





MEDICAL ASPECTS OF NUCLEAR ENERGY



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The Elements of Nuclear Energy

Part One

RADIOACTIVITY

Part Two

NUCLEAR FISSION

Lecture by

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OUTLINE

Part One

RADIOACTIVITY

- 1.00 "Fundamental Particles"
- 1.01 Waves and Particles
- 1.02 The Electron
- 1.03 The Atom
- 1.04 The Proton
- 1.05 Electron Shells
- 1.06 Ionization of an Atom Ions
- 1.07 X-rays
- 1.08 Absorption of X-rays
- 1.09 Natural Radioactivity
- 1.10 The Alpha Particle
- 1.11 Beta Particles
- 1.12 Artificial Radioactivity
- 1.13 The Neutron
- 1.14 The Neutrino
- 1.15 The Positron
- 1.16 The Curie
- 1.17 The Roentgen

Appendix I - Suggested Reading



Part Two

OUTLINE

NUCLEAR FISSION

2.00	The Nucleus
2.01	The Meson
2.02	The Mass-Energy Law
2.03	Bombarding the Nucleus
2.04	A Model of the Fission Process
2.05	The Fission Products
2.06	Neutrons from Fission
2.07	The Chain Reaction
2.08	Plutonium
2.09	The Concept of Critical Size
2.10	The Atomic Bomb
2.11	Atomic Bomb Phenomena
2.12	Health Protection

Appendix I -- Suggested Reading

Appendis II -- Reprint - "Atomic Bomb Explosions"



The Elements of Nuclear Energy

Part One -- RADIOACTIVITY

Sec. 1.00 "Fundamental Particles"

In their search for an understanding of the composition of matter, physicists have had to continually re-define their concepts of the fundamental units of which all matter is constituted. As the quest for the ultimate constituents of matter progressed, it became increasingly apparent that more and more "fundamental particles" were required in order to build up a consistent picture of the atom and its nucleus. At first, it seemed that two particles, namely, the electron and the proton, would suffice to explain the constitution of the elements. Then two more particles — the neutron and the positron — appeared on the horison. Thereafter, in quick succession, two more particles — positively and negatively charged mesons or mesotrons (the names are used interchangeably) were discovered and in the past two years, three new mesons have also come to light, bringing the total to five kinds of mesons. All in all, this adds up to a totality of nine fundamental particles.

Furthermore, there are in addition to these particles, two other fundamental entities which do not conform to the definition of a particle, but behave more like waves. These are the photon and the neutrino. As we shall see later, there is no very distinct line of demarcation between waves and particle; sometimes a particle behaves as though it were a wave and at other times a photon or a neutrino may exhibit what are manifestly properties of a particle.

We shall endeavor to give you some concept of the manner in which this variety of particles is involved in the building-up of atoms and nuclei, so that you may more profoundly appreciate the phenomena associated with radioactivity and fission.

Sec. 1.01 Waves and Particles

Normally one thinks of a particle such as a bullet as being a solid object which rigorously obeys the laws of Newtonian mechanics. One would be surprised if it were pointed out that a bullet, traveling with high speed, has associated with it a "wave length" that we characteristically use to describe a wave phenomenon such as x-radiation or light waves. However, the French physicist, de Broglie, deduced that any particle of mass m and velocity v should have associated with it an equivalent wave length a given by the relation:

$$\lambda = \frac{h}{m \, v} \tag{1}$$

where h is Planck's constant and is numerically equal to 6.6×10^{-27} erg sec.

Now Eq. (1) shows that a small bullet traveling with a high velocity would have an associated de Broglie wave length of about 10⁻³² cm. Such a wave length is of course utterly beyond our present means of measurement, but experience with other phenomena leaves no doubt that the bullet actually possesses this associated wave length.

When we apply our concept of a de Broglie wave to a particle much smaller than a bullet, say, to an electron, then because of the small mass and high velocity of the electron the equivalent wave length is of the order of 10^{-8} cm (or 1 Angstrom unit) and is easily measureable using the techniques of modern physics. You have undoubtedly heard of electron diffraction and can now understand that in this instance, electrons give validity to the principle announced by de Broglie.

It is at first often perplexing to a student that under one set of circumstances a particle should behave precisely as a particle, and under other conditions exhibit wave properties. In reality, any experiment or measurement involves some kind of interaction between the thing being observed and the means by which intelligence is transmitted to the observer. The latter may consist of light rays entering a microscope and striking the observer's eye or they may be x-rays which are recorded by a photographic film, or they may even be electrons which are projected in an electron microscope. In any event the means by which intelligence is conveyed, i.e. the light rays, x-rays, or electrons, must interact with the thing being observed and in the process of this interaction it may exhibit either wave or particle properties depending upon the existing conditions.

Sec. 1.02 The Electron

We shall now proceed to describe the various particles and physical entities introduced in such a rapid-fire manner in Sec. 1.00. From the standpoint of history, the first fundamental particle to be identified and exhaustively investigated was the electron. You are all familiar with the word "electron" but perhaps its properties are not so well known to you. In vacuum tubes, such as those used in any radio, electrons are produced by a hot filament in the tube elements. These electrons are evaporated off the glowing filament by the high temperature which is created in the filament. Careful measurements have shown that all of these

electrons have the same physical properties. Furthermore, electrons produced from a glowing filament are exactly the same as electrons produced by other means, as for example, by release from a photoelectric cell.

The American scientist, Millikan, first showed that an electron is always characterized by a discrete electrical charge of 4.80 x 10⁻¹⁰ electrostatic units. It is significant that this electronic charge, written as -e is the smallest observable bit of electricity. That it is the unit of electric charge is shown by the fact that other particles such as the proton, positron, and meson all have numerically the same value for their charge.

The electron is an extremely light particle, weighing only 9 x 10⁻²⁸ grams. All electrons at rest are found to have exactly the same mass. The vast majority of electrons are not found "free" in nature but are more or less tightly bound within a unit of matter known as an atom. In certain metals we do find very loosely bound electrons; for example, in a conductor such as copper there are many free electrons and when a potential difference (i.e. a voltage) is applied across a section of a copper wire a current of electricity is observed to flow. This electric current is simply the mass migration of the free electrons within the copper.

Sec. 1.03 The Atom

Certainly all of you are familiar with the concept of a chemical element such as gold, tin or hydrogen. An atom is simply the smallest part of a chemical element which enters into a chemical reaction. In this lecture we shall be concerned with events which take place within the atom and it is therefore necessary to talk about the structure and constituents of the atom. For an understanding of atomic structure and for a visualization of a model of an atom, you may find ARMY TALK No. 157, "A NEW WORLD WITHIN THE ATOM" very helpful.

The concept of the atom as a structure which is mostly "space" is one which can be appreciated best by realizing the magnitude of atomic and nuclear dimensions. I gram of hydrogen contains 6 x 10 23 atoms! Thus even if this 1 gram of gas is contained in very large vessel, the number of atoms per cubic centimeter (1 inch equals 2.5 centimeters) is still extremely high. Each hydrogen atom has a diameter of about 10-8 cms (centimeters) which is less than one hundredth millionth of an inch.

We now know that any atom is composed of two parts:

- a) An inner part called the nucleus
- b) An outer part called the electron shell

In order to systematically attack the problem of atomic and nuclear structure, we shall initially confine our discussion to the simplest possible atom. Now the lightest of all the elements is hydrogen and we shall first consider the ordinary hydrogen atom which is known as protium. As some of you may be aware, there is a heavy form of hydrogen called deuterium which we shall discuss later.

Sec. 1.04 The Proton

We conceive of the simplest hydrogen (protium) atom as consisting of a central tiny core or nucleus about which circles a single planetary electron. This core or nucleus of the simplest hydrogen atom is called the proton. A proton is simply a protium nucleus and is formed by stripping off an electron from the lightest hydrogen atom. It should be emphasized that the proton occupies negligible volume inside the hydrogen atom even though it constitutes almost the entire weight of the atom. Its weight is 1840 times greater than that of the electron.

The electric charge carried by a proton is $+4.80 \times 10^{10}$ esu (electrostatic units) or +e, where e denotes the electronic charge. If we add up the charge in a protium atom, we see that the charge on the proton is counter-balanced by the charge on the single planetary electrons, so that the atom as a whole is electrically neutral.

Protons are not normally found free in nature for there is usually such an abundance of electrons everywhere that a free proton would immediately attract an electron and become a neutral hydrogen atom. If, however, we strip off the electron from a hydrogen atom and accelerate it in an evaculated vessel we can momentarily obtain "free protons"; this may be also true in certain regions of intergalactic space.

Sec. 1.05 Electron Shells

Electrons are the only particles which are found within the atom outside of the nucleus and since these electrons are negligibly small in size as compared to the atom, it is clear that the greatest part of the atom is a void. Why then should the atom possess such apparent shape or rigidity which we know from experience it must have? The reason for this lies in the electrical nature of the nucleus as well as that of the electrons which speed about it in never ending orbital paths. In every normal atom, the nucleus carries a positive charge of electricity which is exactly the same as the total negative charge of all the electrons within the atom. This is merely another way of saying that in any neutral atom, the number of protons within the nucleus is exactly equal to the number of orbital electrons.

Between the protons inside the nucleus and the electrons outside of it, there exists an electrostatic force which pulls the particles together. However this force of attraction is just balanced by the centrifugal force due to the whirling motion of the electrons around the nucleus. Thus the electrons perpetually gyrate around the nucleus in orbital paths through the frictionless void of the atom.

Starting with the simplest atom (hydrogen has atomic number 1) the number of orbital electrons is one. The atomic number of any atom is equal to the number of protons in its nucleus. For heavier elements, more and more electrons are found in the orbits. Helium with Z=2 (Z is the atomic number) has two electrons; iron with Z=26 has 26 orbital electrons and uranium has 92 such electrons. These electrons arrange themselves in certain very definite ways about the nucleus and obey rigorous atomic rules. Thus they build themselves up about the atomic core in systematic shells which are peculiar in that each shell can contain just so many electrons. When one shell is filled, the electrons start another shell which is farther away from the nucleus.

These electrons which are in the outermost shell are called the valence electrons. They determine the chemical properties of the atom. Since these outer electrons are farthest from the nucleus, it is reasonable to suppose that these electrons will not be bound so tightly to the atom. The outer electrons are in a sense shielded from the nuclear charge by the inner electron shells so they cannot "see" the nucleus. On the other hand, these electrons in the innermost shell (the innermost shell is called the K shell) are close to the nucleus and are thus more tightly bound to it.

Sec. 1.06 Ionization of an Atom - Ions

If by some means we could pull one of the outermost electrons away from an atom, the resulting atom would no longer be electrically neutral but would have a net charge of +1. The process of removing an electron from an outer shell is called ionization and the resulting atom is called an ion. An atom can be ionized by shooting high speed electrons at it. These minute projectiles may could with some of the outer electrons and knock them out of their orbits away from the atom.

By bombarding an atom with very high energy electrons, it may happen that an electron in a K shell will be knocked out creating a vacancy in it and one of the outer electrons jumps down into the K shell to fill it up. In jumping down (an electronic transition) energy is liberated from the atom in the form of an x-ray.

In general, the ability of a particle to cause ionization depends upon the nature of the particle (i.e. its charge and mass) its velocity, and the state of the medium which it traverses. An electron normally produces about 60 ions per centimeter of air whereas a proton and alpha particle are much more potent, the latter producing tens of thousands of ions per cm of air. In a liquid or solid, more atoms are present per centimeter of the particles path and for this reason more ions per cm are created.

From the viewpoint of the biologist or medical man, the phenomena of ionization is of the greatest importance since it is the ionizing event that serves to initiate the complex series of reactions that characterize radiation damage to tissue. It must be remembered that for any penetrating radiation to cause primary damage to tissue it must produce ionization within the tissue. All charged particles such as protons and electrons readily produce ionization in tissue but x-rays (and gamma rays, for these are identical in nature) are sparsely ionizing and only a relatively few such rays which traverse a layer of tissue will produce ionization; the rest pass harmlessly through the tissue.

Sec. 1.07 X-rays

The emission of an x-ray from an atom always occurs when an electron from an outer shell jumps down to fill a vacancy in a K shell. Because the electrons in different atoms (of different elements) are bound to their respective nuclei with different energy. the energy of the x-ray given off will depend upon the element which is producing them. You have undoubtedly heard of x-ray tubes which have different elements for targets and know that the radiation from a tungsten target is much "harder" than that from a copper target. We have mentioned "hard" radiation but for any real discussion we must specify the radiation more exactly. To do this we can either refer to the energy of the x-ray or to its wave length. Energy is usually measured in terms of electron volts (at least for x-rays). An electron volt is that energy which is acquired by an electron in being accelerated across a potential of 1 volt. In x-ray tubes the electrons emitted by the filament are accelerated by perhaps 100 kilovolts (100,000 volts) and we therefore say that these electrons acquire 100,000 ev (electron volts) of energy. We abbreviate 100,000 ev either as 0.1 Mev (million electron volts) or as 100 Kev. To find the shortest wave length of x-radiation emitted by an x-ray tube operated at V volts, we use the relation:

$$\lambda = \frac{12.345}{V}$$
 in Angstrom units (2)

Using Eq. (2) we see that an x-ray tube operated at an effective voltage of 50,000 volts emits radiation as hard as 0.25 A (A is the abbreviation for the Angstrom unit).

It is, perhaps, more difficult for the student to grasp the physical significance of an x-ray since it does not possess the apparent simplicity of a particle. Physicists are used to speaking of a quantum of x-radiation or of a photon; by this they mean a packet of electromagnetic energy which has an energy that is the product of Planck's constant (h) and the velocity of light (c) all divided by the wave length of the radiation. Thus:

$$E = \frac{h c}{\lambda}$$
 (3)

If we thus define the wave length of any x-ray, we also state its energy as given in Eq. (3).

Sec. 1.08 Absorption of X-rays

X-rays are, by themselves, not ionizing. They can produce ionization only after they interact with matter to produce a high speed electron by one of the following processes:

- 1. Photoelectric Effect in which case the x-ray interacts with an atomic electron and ejects it from its parent atom. The photoelectron thus ejected carries off the energy of the incident photon and produces ionization characteristic of any electron of that energy. In the process the incident photon is completely absorbed and disappears.
- 2. Compton Effect wherein the x-ray quantum behaves as though it were a particle and collides with an atomic electron ejecting it (Compton recoil electron) from the atom. This recoil electron does not carry off all the energy of the incident photon for the photon survives the collision but is reduced in energy (i.e. made of longer wave length).
- high energy photons interact with atoms (near the nucleus) and completely give up their energy to form a pair of electrons. One electron is the ordinary negatively charged type (negatron) that we have already discussed but the other is a new type called a positron (see Sec. 1.). The latter is the same as an ordinary electron except that it is positively charged and has a transitory existence.

These three effects vary in importance depending upon the energy of the photon considered and the nature of the absorbing

material. A given x-ray quantum may traverse a considerable quantity of matter before it interacts with an atom and gives up its energy. Thus, there is no definite distance or range that an x-ray of a given energy travels before it is absorbed. There is, however, a quantity, known as the half-thickness that can be used to describe the gross absorption of x-rays in matter. The half-thickness $(x\frac{1}{2})$ is that thickness of material which is just sufficient to reduce the intensity of an x-ray beam by a factor of two. For example, the half-thickness of lead for 1.0 MeV x-rays is 0.87 cm. This means that 0.37 cm of Pb will absorb 50% of the 1.0 MeV x-rays incident upon it; similarly 1.74 cm of Pb will reduce the intensity of the same x-ray beam by a factor of 4. Doubling the thickness of material produces 4 times as effective a shield for the same energy x-radiation.

1.09 Natural Radioactivity

About 50 years ago physicists found that certain elements such as uranium and radium give off penetrating radiation. The radiation emitted by these radioactive elements was not immediately separated into its component parts and identified, but today we know that the naturally occurring radioactive elements emit three kinds of radiation:

- 1. Alpha particles (See Sec. 1.10)
- 2. Beta particles (High speed negative electrons)
- 3. Gamma rays

All the various radioelements can be grouped into three major series of elements, namely the uranium, the thorium and the actinium series.

Because of its great penetrating power, the gamma radiation was the object of much investigation by research workers. We now know that gamma rays are photons or quanta having exactly the same properties as x-rays. Except that the two arise from a different site within the atom, they are identical in their nature. Thus gamma radiation is absorbed by the same mechanisms as hold for x-rays. Actually gamma rays arise from excitation of nuclei as will become clearer in the following sections:

When a member of a radioactive series undergoes a disintegration or decay, we describe this process most succinctly by using equations. In order to understand the equations involved in these radioactive transformations, we introduce the following nomenclature:

Z = atomic number i.e. the number of protons in the nucleus A = mass number i.e. the sum of the nucleons*in a nucleus

n = symbol for a neutron

Hl or p = sumbol for a proton

e or or e = negative electrons

e or or or e = positron

^{*} The term nucleon refers to either a neutron and/or proton in a nucleus.

Any element of atomic number 3 may have more than 1 mass number associated with it, i.e. have more than 1 isotope, so that we have to specify the exact mass value for any given value of 3. We do this by writing the chemical symbol of the element, adding a superscript to indicate the mass number and for convenience, a subscript for the atomic number. Thus

the proton is written as 1H the deuteron (a deuterium nucleus) as 1H and the gold nucleus as Au'??

More generally, Mass Number

(Chem. Symbol) or Atomic Number

Sec. 1.10 The Alpha Particle

If a quantity of pure radium is sealed in a glass tube and allowed to stand for some months, it is found that a gas accumulates within the tube. By spectroscopic means, this gas has been identified as the noble gas, helium. Now we know that helium is the simplest of all elements except hydrogen and we conclude that the radioactive decay of radium must involve the emission of helium nuclei (or alpha particles). We express this radioactive transformation as follows:

Here the emission of an alpha parti e reduces the atomic number of radium by 2 units and the mass number by 4 units and we see that equation (4) is balanced, so far as subscripts and superscripts are concerned, in much the same manner as in an ordinary chemical equation. The new element radon, formed in the decay of radium, is also unstable and proceeds to decay forming an isotope of element 84, (polonium). The latter is also radioactive and decays by alpha emission to form an isotope of lead. We can thus piece together a series of transformations, all of which are intimately related and form part of the uranium series. This part of the series is shown as

where the symbol & (alpha) is used to denote the emission of an alpha particle. Scientists commonly call the decaying isotope, the "parent" and the decay product, the "daughter".

As emitted from nuclei alpha particles have of the order of 5 Mev of energy and therefore move with high velocity. They simply are particles composed of 2 neutrons and 2 protons and compared to electrons, such nuclei are massive and might be expected to be easily absorbed in matter. This is really the case for most alpha particles are completely stopped by a few sheets of thin paper. We shall see later that this very short range of action for an alpha particle does not prevent it from being effective in damaging cell tissue.

Sec. 1.11 Beta Particles

Lead is commonly thought of as a very stable element. By that we mean that it does not undergo radioactive decay. However, the isotope of lead which is formed in the radioactive series (Eq. 5) is not stable. It has 214 nucleons in its nucleus and since it must have 82 protons, there are 214-82 or 132 neutrons in its nucleus. Now of the lead atoms found, in nature the heaviest isotope is 82Pb 208. Thus the isotope 82Pb214 is much heavier than the heaviest natural lead isotope for it contains six additional neutrons. Instead of emitting an alpha particle which would make the neutron surplus even worse, the lead isotope 82Pb214 emits a beta particle and the reaction is as follows:

In this case, lead changes to an element of higher atomic number since the emission of an electron is equivalent to adding a charge of the to the lead nucleus. In these nuclear reactions electric charge is always equal on each side of the equation i.e., charge is conserved. Since the electron has negligible mass the atomic weight of the isotope of bismuth is the same as the parent atom. By succeeding 3-and &-emissions the bismuth atom is finally transformed to a stable isotope of lead (82Pb206). This isotope then terminates this series. In addition, the two naturally radioactive series, the thorium and the actinium series, both finally decay to stable isotopes of lead.

When they are emitted from radioactive nuclei, beta particles have of the order of 1 Mev energy and thus move with very high velocity. In spite of their high velocity these electrons are easily stopped in matter. Most beta particles have a range of a few millimeters in water and only the most energetic penetrate more than a few millimeters of aluminum. In contrast to the absorption of gamma rays, both alpha and beta particles have a rather definite range in matter and are easily stopped in relatively small thicknesses of shield.

Later on, in Sec. 1.14 we discuss the mechanism of the emission of beta particles. At this point, however, the student may be puzzled as to the origin of these beta particles for we have only spoken of neutrons and protons as making up the nuclei of atoms. One must think of the process of beta-decay as similar to that of x-ray emission in that the beta particle is created in the emission process analogous to the formation of an x-ray.

Sec. 1.12 Artificial Radioactivity

If a nucleus of an atom is subjected to bombardment by charged particles, such as protons, deutrons, or alpha particles, which have been artificially accelerated to high velocity in a cyclotron or similar machine, it is possible that some of the bombarding particles will make a collision with target nuclei and a nuclear reaction may occur. In some instances, the nucleus of the target material may be simply "excited" by the bombarding particle and it may return to its normal state by the emission of a photon of appropriate energy. In other cases, the nucleus may undergo a radioactive transformation to form an isotope of another element. In general, substances which are thus made artificially radioactive decay either by emission of gamma rays, or by beta-decay; in some cases a neutron may be emitted but in this instance the reaction is an instantaneous one.

Artificial radioactivity may also be induced in many elements by bombarding them with a beam of neutrons.

Certain nuclei, made artificially radioactive, by bombardment with charged particles have also been found to emit positrons. (See Sec. 1.15).

Sec. 1.13 The Neutron

Prior to 1932, when the proton and electron were the particles used to explain the constitution of nuclei, theoreticians were unsuccessful in their attempts to account for the postulated presence of electrons within nuclei and for the disagreement of predicted and measured values for nuclear constants. In 1932 an English physicist discovered a new particle known as the neutron which was immediately used to successfully explain the physical constitution of nuclei. Chadwick produced neutrons by bombarding beryllium with natural alpha particles. This reaction is illustrated as

$$4^{\text{Be}^9} + 2^{\text{He}^4} + 6^{\text{Cl}^2} + 0^{\text{nl}}$$
 (7)

The neutron is actually slightly heavier than a proton weighing 1.008937 mass units in comparison to 1.007581 m.u. for a proton.

We conceive of any nucleus of mass number A and atomic number Z as made up of N neutrons and Z protons. Obviously N must equal A-Z.

The neutron does not enjoy a "free" existence outside the nucleus for it is itself unstable and decays according to the reaction.

$$0^{n^{1}} \longrightarrow 1^{H^{1}} + -1^{e^{0}} + \eta^{n}$$
(8)

where the symbol. 7 (Greek eta) is used to denote a new entity called the neutrino (see Sec. 1.14).

In contrast with charged particles which must ordinarily have high energy in order to initiate nuclear reactions, the neutron is a particularly useful particle at even very low (i.e. \(\frac{1}{30} \) e.v.) energy.

Sec. 1.14 The Neutrino

Our previous discussion of beta particles did not postulate a mechanism for their emission from nuclei. The beta particles emitted from a radioactive element such as carbon-14 (C14) are not all of the same energy but exhibit a distribution of energies with a maximum number of beta particles having about one-third the maximum (E_{Max}) energy. Obviously, we must somehow account for the energy which a nucleus has available for beta decay. If in a given decay, a beta particle carries away energy less than E_{Max}, where then does the rest of the energy go? Careful experiments have shown that it is not emitted in the form of gamma radiation so that a major nuclear mystery is at hand. To solve this baffling problem. Pauli postulated the existence of a neutral "particle" of almost zero rest mass which is emitted during the process of beta decay—this particle is called a neutrino and is written as η° where the sub—and superscripts indicate it has zero mass and no charge.

There is very little direct experimental evidence to substantiate the existence of a neutrino and although some experiments support the neutrino hypothesis, we must regard the evidence as supporting rather than proving the existence of the neutrino. Once emitted the neutrino does not interact with matter or if it does so this interaction is not measureable - we might say that the half-thickness for absorption is several light-years of lead!

Sec. 1.15 The Positron

Certain nuclei, such as Cu⁶⁴ are observed to emit positive electrons (positrons), a reaction which we describe by the equation

$$29^{\text{Cu}^{64}} \longrightarrow 28^{\text{Ni}^{64}} + +1^{\text{e}^{\circ}} + \circ \gamma^{\circ}$$
 (9)

Here again in order to account for the observed phenomena, we postulate that a neutrino is emitted. Once emitted, the positron lives only for a few millionths of a second for it is quickly absorbed in matter (in pure space it would live forever) by a bizarre reaction known as annihilation. In this unusual process, the positron interacts with an electron and there transforms itself into two quanta of energy. We indicate this reaction as follows:

$$+1^{\circ}$$
 $+1^{\circ}$ \longrightarrow 2 Gamma rays (10)

Thus two particles are destroyed in the annihilation process to create a pair of gamma rays. As we shall see in Part Two, matter and energy are interconvertible according to the Einstein relation E- mc². In this process two electron masses, equivalent when at rest to 1.02 Mev energy, produce two 0.51 Mev gamma rays.

Instead of decaying by positron-emission, the Cu⁶⁴ nucleus may swallow up (it might be called a cannibal nucleus) one of its own K-electrons in a process known as K-capture. Thus

$$29^{\text{Cu}^{64}} + _{-1}^{\text{eo}} \rightarrow 28^{\text{Ni}^{64}} + _{0}^{\text{eo}}$$
 (11)

The same end product nucleus (Ni⁶⁴) results as given in Eq (9).

Sec. 1.16 The Curie

You have probably been wondering about the time scale on which these radioactive transformations take place. Does the radium atom, for example, disintegrate in 1 second or in 1 year? Actually the process is statistical in nature and if we were able to look at one isolated radium atom, we might see it decay in a minute or we migh have to wait a million years for it to disintegrate. If, however, we look at 1 gram of radium atoms, we see that there are so many atoms (23-3 x 10²¹ atoms) that there is an average value for the time during which 50% of these atoms will decay. This time is called the half life and for radium it is 1600 years. If we start out with one gram of radium, then in 1600 years we will have only one half gram on hand.

Radium is said to be long-lived but other atoms have extremely short half lives of the order of one-millionth of a second. Still others like 92^{0238} (the heavy isotope of uranium) is very long lived, having a half life of 4.5 x 10^9 years.

In order to calculate the activity of any sample of a radioactive material we multiply the number of atoms present as follows:

Activity = (No. of Atoms) (.69) = disintegrations per second

Suppose we calculate the activity of 1 gram of radium. Now 226 grams of radium are equal to 6×10^{23} atoms so 1 gram is 2.6 x 10^{21} atoms and since the half life is 1600 years or 5×10^{10} seconds

Activity of 1 gm of Ra == (2.6×10^{21}) (.69) ==3.7 x10¹⁰

disintegrations/second.

In practice this activity is called the <u>curie</u> and is an accepted standard unit. You are perhaps familiar with the millicurie (mc) unit which is one thousand times smaller than the curie. A new unit, known as the rutherford, abbreviated rd, is defined as the quantity of a radioisotope that disintegrates at the rate of one million disintegrations per second (i.e. 10^o dis/s).

Sec. 1.17 The Roentgen

In treating a patient with 7 radiation from a radium capsule it is necessary to measure the dose which is given. For this purpose we use a unit called the Roentgen named after the discoverer of x-rays. The Roentgen abbreviated is r and is defined as that quantity of x-radiation which on passing through 1 cubic centimeter of normal air produces 1 electrostatic unit of ions. While it was originally defined only for x-rays, the definition is equally valid for gamma rays. A smaller unit, the milliroentgen (mr) is often used in practice. The definition is perhaps not too meaningful to you because of the term "electrostatic unit" which is used. Physically, one should think of the definition as meaning that the quantity of x-rays which is measured by a certain number of ions produced in a standard volume of air. Quantitatively, 1 roentgen is equivalent to 2.083 x 109 ion pairs per cc of standard air. Other equivalences are

1 r = 1.61 x 10¹² ion pairs/gram air 1 r = 6.77 x 10 Mev/cc air 1 r = 83.8 erg/gram air

Later on you will see that different types of instruments can be used to measure x-radiation. These are ionization chambers, Geiger-Muller counters, and photographic emulsions. One should sharply distinguish between two types of measurements --

A -- Those that measure the dose or total quantity of radiation.

B -- Those which give the dose-rate or the intensity of radiation.

Dose is measured in roentgens whereas dose-rate is measured in terms of roentgens/second or roentgens/minute or in other time units. It is one thing to give a patient a dose of 1 r or x-rays and quite another to expose a patient to a dose-rate of 1 r/second. In the latter case, the patient receives a 1 roentgen dose in one second and a 60 roentgens dose in 1 minute. In one hour the patient would be dead or would be as good as dead.

APPENDIX I

Suggested Reading - Radioactivity

A. Books

Brown, T. B. Foundation of Modern Physics New York: Wiley (1948)

Cork, J. M. Hadioactivity and Nuclear Physics
New York: Van Nostrand (1947)

Hoag, J. B. and S. A. Korff Electron and Nuclear Physics
New York: Van Nostrand (1948)

Jauncey, G. E. M. Modern Physics
New York: Van Nostrand (1948)

Lapp, R. E. and H. L. Andrews Nuclear Radiation Physics
New York: Prentice-Hall (1948)

Rasetti, F. Elements of Nuclear Physics New York: Prentice-Hall (1936)

Richtmyer, F. K. and E. H. Kennard Introduction to Modern Physics New York: McGraw-Hill (1948)

Semat, H. Introduction to Atomic Physics
New York: Rinehart (1946)

Stranathan, J. D. The "Particles" of Modern Physics Philadelphia: Blakiston (1942)

B. Literature

Cassen, B. "X-rays in Medicine" Review of Modern Physics 12, 405 (1941)

Compton, A. H. "The Corpuscular Properties of Light"

Review of Modern Physics

1, 74, (1929)

Evans, R. D. "Radioactivity Units and Standards" Nucleonics 1, 32 (Oct. 1947)

Gamow, G. "The Reality of Neutrinos" Physics Today
1, 4 (July 1948)

Gray, G. W. "The Ultimate Particles" Scientific American 178, 26 (1948)

Halliday, D. "The Special Theory of Relativity in Nucleonics"

Nucleonics

2, 60 (Mar. 1948)

Jauncey, G. E. M. "Early Years of Radioactivity"

American Journal of Physics 14, 226 (1946)

Lapp, R. E. and H. L. Andrews

Atomic Structure

Proceedings of The Institute
of Radio Engineering
36, 1068 (1948)

* Reprints available from Dr. H. L. Andrews,
National Institute of Health
Bethesda, Maryland

Seaborg, G. T. "Artificial Radioactive Tracers" Science

Seaborg, G. T. "Artificial Radioactivity" Chemical Review
27, 199 (1947)

Wheeler, J. A. "Elementary Particle Physics" American Scientist
35, 177 (1947)

NUCLEAR FISSION

Sec. 2.00 The Nucleus

We have already given some description in Part One of the constitution of the nucleus but as yet we have not given any explanation of the forces operating within the nucleus, neither have we discussed the nature of the meson. As it happens, the two are intimately related for the meson is postulated to be a particle that is "exchanged" between a pair of nucleons within a nucleus and thus binds them together. In the next section we shall have more to say about mesons; for the present let us confine our attention to the neutrons and protons within the nucleus.

The central core or nucleus of an atom is a dense aggregrate of nucleons all of which are in a constant state of agitation and rapid motion. We liken the nucleus to a liquid drop in which the nucleons are bound to each other by short range nuclear forces. By using the words "nuclear forces" we refer to the queer type of forces that are exerted between nucleons and keep the nucleus together. Other types of forces, such as gravitation or electrostatic, are utterly incapable of explaining the magnitude of the energy bound up within the nucleus. We are thus forced to assume the existence of a nuclear force that is effective over a very short range (about 10-13 cm) and is negligible outside the nucleus.

All nuclei are of practically negligible volume in an atom when compared to the total volume of the atom as define by its outermost electron shell. Furthermore a nucleus of aluminum is not very much smaller than that of the heaviest naturally occurring isotope, i.e. U^{238} . If we imagine an atom viewed in cross section, the atom itself has an area of about 10^{-16} sq. cm. whereas the nucleus occupies only about 10^{-24} sq. cm. Physicists often refer to the unit of 10^{-24} sq. cm. as a barn.

Sec. 2.01 The Meson

At this stage in the student's development it may seem unduly sophisticated to introduce any discussion of the meson and we do so with the assumption that he will skip quickly to the next section should he be too confused by the nature of the unusual particle.

There are two distinct kinds of mesons (or mesotrons); a heavy kind having a mass about 300 times that of an electron and a light or ordinary kind that is found in the cosmic radiation. The light meson has a mass about 200 electronic masses and in common with the heavier type occurs both as a positively charged particle and also as one bearing a negative charge equal to that carried by

an electron. In this discussion we shall consider only the heaviest mesons for they are the ones which are involved in nuclear forces. These mesons are extremely unstable and decay in about 4 x 10-8 seconds. Normally they are not found outside the limits of the nucleus. Theoretical physicists assume that a neutron within a nucleus changes into a proton, and similarly a proton into a neutron, by the emission of a positive or negative meson respectively. These interchanges of identity of the nucleons occur with extreme rapidity and the meson thus acts as an exchange particle serving to bind a pair of nucleons together.

Sec. 2.02 The Mass-Energy Law

The relation $E = mc^2$, first announced by Einstein, achieved front-page headlines with the detonation of an atomic bomb over the city of Hiroshima. In an atomic bomb detonation a large number of uranium-235 or plutonium-239 (a transuranium element manufactured from U^{238}) nuclei are split in two parts or <u>fissioned</u>. Splitting of a compact heavy nucleus into two approximately equal parts serves to convert an appreciable amount of mass, actually about $\frac{1}{4}$ mass unit, into energy. Let us now apply the Einstein equation to a single fission process and calculate the energy released. 1 mass unit is about the weight of one proton or one neutron and is equal to 1.6 x 10^{-24} grams. Therefore $\frac{1}{4}$ mass unit is 0.4 x 10^{-24} grams and the energy equivalent to it is simply

$$(0.4 \times 10^{-24}) \times (3 \times 10^{10})^2$$

where 3 x 10^{10} cm/sec is the velocity of light. Multiplying, we see that this product equals 3.6 x 10^{-4} ergs. To convert to electron volts, we must multiply ergs by a factor 6.25 x 10^{11} . This multiplication yields 230 MeV (million eV). Thus the fission of a single U^{235} nucleus yields roughly 200 MeV of energy. However, the original unfissioned U^{235} nucleus is itself equivalent to a total energy of about 220,000 MeV so that per fission we realize a release of only 200/220,000 or one-thousandth of the total energy.

The reader will recall from his freshman physics course that a fundamental law of motion is stated as

In this statement of the relation, it is assumed that the mass of the thing being accelerated is a constant and does not depend upon its velocity. Whenever one is dealing with large masses or low velocities, this law is strictly valid but for the very minute nuclear particles the law fails to hold for high velocities. To be strictly true the law must be restated to read:

force . the time rate of change of momentum (2)

where momentum is equal to the product of mass times velocity and it is allowed that mass may depend on velocity. The dependence of mass on velocity is given by the relativistic equation

$$m = 0$$

$$\sqrt{1 - \frac{(v)^2}{(c)}}$$
(3)

where mo is the mass of the particle at rest

m is the mass of the particle when moving at velocity v

c is the velocity of light.

an electron in a television tube may be accelerated by a voltage of 50,000 volts and thus attain a velocity about 0.4 that of the velocity of light; in so doing it becomes 10% heavier than when at rest. If an electron is accelerated by 0.5 million volts, as in a high-voltage x-ray tube, it becomes twice as heavy as an electron at rest.

2.03 Bombarding the Nucleus

We have already postulated that the nuclear forces are such that their effect, or more precisely termed their field i.e. area of influence, is confined to the nucleus. However, the protons inside the nucleus make themselves known outside the confines of the nucleus by their electrostatic "field". This "field" forms a barrier around the nucleus which prevents any charged particles from entering the nucleus. If, however, the particle which seeks to enter it is uncharged, it cannot see the particle and offers no resistance to its entry. For this reason, neutrons of low energy can easily slip inside the nucleus whereas protons of very high velocity are barred. Every technique that man has devised for producing high energy charged particles involves considerable equipment and operational cost far in excess of the energies generated by the nuclear reactions which are produced by the bombardment.

In any bombardment of a target with a beam of charged particles we find that the number of "hits" made by the bombarding particles are small in comparison to the number of particles in the incident beam. The reason for this low "batting average" is that the nucleus is such an infinitesimal part of the atom that it exposes very little target surface to the bombarding missile. If we consider only the geometrical cross-section of the nucleus (i.e. 10^{-24} sq. cm.) then we see that the chance that an incident particle will strike in this area is $10^{-24}/10^{-16}$ where the denominator is the area of a single atom; this means that the probability is only 1 in 100,000,000 that the particle will score a "hit". Actually this probability is somewhat higher since a single particle may pass

through many layers of atoms, say, a 100, so that only one incident particle out of every million produces a "hit".

It is a peculiar property of the neutron that it produces nuclear reactions with a much higher probability than do charged particles. Another way of saying this same thing, is to state that some nuclei have an extremely large "cross section" for neutron-induced reactions. These cross sections may be 500, 1000, or 10,000 (and even higher) barns; this, in effect, means that the nucleus presents a virtual cross sectional area for the neutron far larger than its geometrical area. One of the reactions which has such a high cross section is that of nuclear fission in the heavy elements.

2.04 A Model of the Fission Process

A few very heavy nuclei, such as U-235, when bombarded by slow neutrons react very violently by splitting into two almost equal parts. The process is called nuclear fission or simply fission and the isotopes which exhibit this unusual behavior are called fissionable. The heavy products of the fission reaction, i.e. the two halves of the heavy atom are known as fission products or fission fragments.

We can picture the fission process by bringing into consideration the liquid drop model of the nucleus which we have just discussed. Let us imagine that before the neutron enters the uranium 235 nucleus all the 92 protons and 143 neutrons are in constant motion inside the spherical nucleus. Let us assume that because these nucleons are so close together and move about so rapidly. that they lose their individual identity and may be thought of as forming a fluid or liquid drop of uniform density. With the intrusion of a neutron into this contented system, the liquid drop has energy added to it and becomes excited. The particles inside the nucleus are set into more violent motion and the drop begins to lose its spherical shape. As it deforms into a non-spherical shape it sets up rapid oscillations which deform it still further into a dumbbell pattern. At this point the original sphere is essentially drawn out into two smaller spheres with a tenuous connecting link which then snaps. Then the two fission products shoot away from each other with high velocity. All this happens in an exceedingly short time interval of less than 10-12 seconds.

Of the 200 Mev of energy released in a single fission process the majority of the energy goes into energy of motion of the fission fragments (kinetic energy). If the material undergoing fission is in the form of a metal, then the fission fragments will travel only a very short distance before they lose their energy. In this short distance the kinetic energy of the fission product is imparted to other surrounding atoms which then are excited to higher speeds.

Thus if a sufficient number of fissions occur per unit volume of the metal, then the totality of the unfissioned atoms will be increased in their kinetic energy and as a result the temperature of the mass will increase proportionately to the number of fissions taking place. Whether or not the energy is released in an atomic bomb explosion or in an atomic power plant, the source of energy is the same, namely, in the heat energy produced by the fission fragments.

2.05 The Fission Products

It would be rare for a pair of fission products to have the same mass and we know that it is much more common for one of the products to be heavier than the other. In general, there are two groups of fission products, one with an average mass number of about 95 and the other of about 139. Just why the two fragments are unequal in mass, we do not know.

We do know, however, that the fission products are intensly radioactive, emitting high-energy beta particles and gamma rays. By emitting /3-particles, the isotopes which contain too many neutrons (or too few protons) tend to make themselves more normal since /3-emission is equivalent to changing a nuclear neutron into a proton. Because the fission products are born with such extreme neutron excesses (or proton deficits) it requires four or five separate /3-decays to result in stable atoms. Thus each fission product is often associated with a chain of radioactive isotopes and for this reason we speak of fission chains. Almost all fission products emit very penetrating gamma rays in addition to beta particles. The half lives for the various fission products vary from a fraction of a second to many years.

The result of fissioning a large number of atoms is that we have an aggregate of many different fission products representing almost every element from atomic number 40 to 70. This fact makes the chemical decontamination of fission products a very difficult task.

If we were to assume that a U²³⁵ is split into fission products of exactly the same mass and atomic number, then we would have two Pd¹¹⁸ nuclei (Pd is the symbol for palladium). The heaviest naturally occurring isotope of this element is Pd¹¹⁰ so we see that such a fission product as Pd¹¹⁸ would have a neutron excess of 8 neutrons as compared to Pd¹¹⁰. As we have just explained this neutron excess can be relieved by successive emissions of beta particles from the fission product nucleus. One might wonder, however, if an alternate process might occur: could not the fission product emit a neutron?

2.06 Neutrons from Fission

Actually neutrons are observed to be emitted in fission. Work by Zinn and Szilard (see reference 15) has shown that an average of 2.3 neutrons are emitted per fission. Over 99% of these

neutrons are prompt, i.e. emitted within an extremely short time of less than 10^{-10} seconds, but even so it has been shown that these neutrons are emitted by the fission products. There are some (less than 1%) of the neutrons which are not prompt but are <u>delayed</u> in emission by 10, 15, 30, and 45 seconds. These delayed neutrons are of extreme importance in the application of nuclear fission in a <u>chain reactor</u> or <u>pile</u>. Only a very few of the fission products are are known to emit delayed neutrons and the longest half life observed for delayed emission is 1 minute.

In addition to the neutrons emitted from fission, there are rarer events associated with the fission process. Sometimes, perhaps once per thousand fissions, the nucleus fissions into three fragments rather than into the customary pair of fission products. Furthermore, high energy alpha particles sometimes accompany the fission process. One should remember that these are rare events and do not alter our simple picture of the fission process as given in Sec. 2.04.

2.07 The Chain Reaction

If we wish to talk about the fission of large numbers of uranium atoms, it is necessary to have large numbers of neutrons available. Because the fission process requires only one neutron to initiate it and yet gives off between two and three neutrons per fission, it is possible to use fission neutrons to start a "chain" of fission reactions. Each fission adds more neutrons to the reaction so that more and more reactions are possible. Such reactions are called self-sustaining or chain reactions.

Since the fission process occurs so quickly, it is conceivable that if we were to properly assembly a certain "critical" mass of fissionable material such as U-235, we could set off a series of fissions which would proceed so quickly that the recoiling fission products and radiations would raise the critical mass to a multimillion degree temperature within a fraction of a second. By definition, such a process would be explosive in nature.

Prior to World War II, no pure U-235 was available. Ordinary uranium metal contains 140 times more U-238 than it does U-235. Now U-238 is not suitable for a chain reaction because when it absorbs a neutron into its nucleus, it merely changes into a heavier element without fissioning. Since the two isotopes of uranium are chemically identical, they had to be separated by exceedingly difficult physical methods. In fact, the methods presented so many technical obstacles, that the Manhattan Project set up huge plants which used nuclear reactors running on natural uranium to generate a new man-made fissionable material——plutonium.

2.08 Plutonium

With neutrons released in the fission of the small amount of U-235 present in natural uranium metal, it was possible to sustain a chain reaction in a pile of graphite and uranium. Under proper conditions a large number of these fission neutrons can be absorbed by the U-238 atoms. This results in an unstable U-239 nucleus which rapidly decays by beta emission as follows:

$$92^{U^{238}} + o^{n^{1}} \longrightarrow 92^{U^{239}} \longrightarrow 93^{Np^{239}} + -1^{e^{0}}$$
 (4)

Here Np is the symbol for the new transuranium element neptunium. Neptunium is itself radioactive and soon decays to form an isotope of element 94 which has been named plutonium. Thus

$$93^{\text{Np}^{239}} \xrightarrow{2.3\text{d}} 94^{\text{Pu}^{239}} + -1^{\text{e}^{\circ}}$$
 (5)

The figure 2.3d over the arrow means that this reaction has a half life of 2.3 days.

Plutonium is a dense silvery metal similar to uranium U-235 in that it is fissionable with slow neutrons (i.e. neutrons which are of low energy). Like U-235 it is also an alpha emitter but since it has a half life of 24,000 years, it is much more active than U-235 which has a half life of 7×10^8 years. The alpha activity of plutonium is sufficiently intense so that it constitutes a dangerous health hazard of about the same order as radium when it is deposited in bone matter.

2.09 The Concept of Critical Size

One of the unique characteristics of an atomic explosive is that it must be assembled into a certain <u>critical size</u> before it can explode. The reason for this unusual characteristic is that the chain reaction will not be a self-perpetuating one unless there are sufficient neutrons to cause continued fission. Suppose, for

example, we wish to run a chain reaction at a rate of 500 fissions per second. Suppose, further, that each fission generates exactly two neutrons. This requires that one out of every two neutrons generated must be used to produce more fissions, so that we have to have 500 neutrons being used every second to cause fission. This leaves an additional 500 neutrons which we can afford to "lose" from our system either by absorption (not leading to fission) or by loss through escape from the system. By increasing the amount of fissionable material in the assembly, we finally succeed in overcoming the loss of neutrons and the system becomes supercritical and self-sustaining.

If we know the number of fissions occurring per unit time in a reactor we can immediately deduce the power level of operation by using the relation that 1 watt of power is equal to 3×10^{10} fissions/second. Thus in a 1000 kilowatt pile 3×10^{16} atoms are fissioned each second and in one day's operation $86,400 \times 3 \times 10^{16}$ or 2.5×10^{21} atoms are fissioned. To convert this figure into grams of U^{235} consumed per day, we multiply by the mass number -235 and divide by Avagadro's number--- 6×10^{23} . This yields a result that 1 gram of U^{235} is fissioned per day and, of course, 1 gram of fission products is produced per day.

2.10 The Atomic Bomb

A logical way to assemble an atomic bomb might be to take two hemispheres of fissionable material each of which is sub-critical and bring them very quickly together to form an over-critical mass. A gadget which might accomplish this result is shown in the projected diagram. One hemisphere of pure U-235 might be imbedded in a large mass of material (tamper) placed at the target end of a gun barrel. At the other end of the barrel might be another hemisphere which serves as a projectile. Separated by the length of the gun barrel, each hemisphere would be sub-critical and safe, but by firing the one hemisphere down the barrel, it would attain a high velocity and weld itself together with the target into an over-critical mass. The inertia of the projectile together with an appreciable length of time of contact would be necessary so that a large amount of the uranium would be fissioned. This might insure a high "efficiency" for the reaction. No data are available to specify a value for this efficiency.

The value for a critical mass of U^{235} or Pu^{239} is secret but we can easily calculate the value of the amount of U^{235} that is fissioned in an atomic detonation given as equivalent to 20,000 tons of high explosive—this value is the product of the amount of fissionable material used in the bomb multiplied by the efficiency of the gross fission process. Now 20,000 tons of high explosive are

equal to 1.8 x 10^{13} calories or 4.8 x 10^{26} MeV. We know that each fission releases about 200 MeV of energy, about 85% of which is released in the form of heat. This means that 20,000 tons of high explosive = $\frac{4.8 \times 10^{26}}{170}$ = 2.8 x 10^{24} U²³⁵ atoms fissioned. The

latter is equal to 1100 gms of U235 or roughly 1 kilogram of U235.

2.11 Atomic Bomb Phenomena

In Appendix II, the reader will find a treatment of the various effects associated with the detonation of an atomic bomb. One should bear in mind that there are the instantaneous or prompt effects as well as the prolonged or what may be called the long-term effects. Each effect is sensitive to the conditions under which the bomb is exploded. Thus a high air burst leaves little or no residual radioactivity in the vicinity of the bomb burst whereas an underwater explosion is certain to produce severe local contamination.

Wherever radioactive contamination occurs, the area must be carefully surveyed with reliable radiation measurement instruments in order to determine the nature and degree of the radioactive hazard. Thereupon the data obtained must be reviewed and interpreted by a trained health physicist or radiological safety officer in order to insure that personnel admitted to the area are not unduly exposed to radioactivity.

2.12 Health Protection

In the case of fission products or other radioactive material which is deposited on a surface, we may divide up the hazards into two categories:

A. The External Hazard

Because of the extreme penetrating power of gamma rays, any source emitting these rays may constitute an external hazard even though the source is considerably removed from the site of exposure. Long experience with x-radiation has led to a permissible dose rate of 0.1 roentgen per day. Setting up a figure of 0.1 r/day should not be interpreted as giving personnel license to receive this full amount of radiation per day; wherever possible, operations should be conducted so that the minimum amount of dose is received. Present indications are that a dose of 0.1r per day received 5 days a week for long periods of time is not harmful to personnel, but we caution that too little is known of the long-term chronic effects of penetrating radiation to regard this permissible dose rate as absolute. If a pharmacologist assures you that a daily dose of so many grains of arsenic is not injurious to the human system, we are certain that

you will not be tempted to take that much arsenic on a daily basis; the same caution should apply to nuclear radiation.

B. The Internal Hazard

Should radioactive emitters gain entrance into the body. either through ingestion or inhalation or by other means, they may be retained in the body and constitute an internal radioactive hazard. Whereas alpha and beta particles rarely consitute a source of external hazard, when they are emitted in the body they may create intense ionization in localized areas, such as bone marrow, where they may do irreparable damage to vital cell structures. Furthermore, since the emitters may lodge deep within the body and be difficult to identify with health monitoring instruments, the hazard is all the more insidious. For this reason, health physicists set up certain tolerance concentrations for specific isotopes in air and in liquids, and systematically monitor these media to prevent exposure of personnel to dangerous hazards. The actual quantity of a given radioelement that can be tolerated without damage to the body depends upon the chemical form of the element, the percentage uptake by the body, the rate of excretion from the body, the physical characteristics of the isotope (half-life, particle emitted, energy of radiation, etc.), and the site where the radioelement lays down in the body.

Lest the reader feel undue apprehension about the feasibility of large scale work with radioactive material, let us point out that given proper health surveillance and monitoring equipment, operations with even very large quantities of radioactivity may be carried out safely. But because radioactive hazards must be detected by instruments sensitive to them (nature not having seen fit to endow man with faculties to sense nuclear radiation) we must be ever alert to the potential of radioactive hazards.

APPENDIX I

Suggested Reading - Nuclear Fission

A. Books

- Goodman, C. D., <u>The Science and Engineering of Nuclear Power</u>

 Cambridge: Addison-Wesley Press (1947)
- Hume-Rothery, W., Atomic Theory

 London: Institute of Metals (1947)
- Lapp, R. E. and H. L. Andrews, <u>Nuclear Radiation Physics</u>

 New York: Prentice-Hall (1948)
- Powell, C. G. and G. P. S. Occhialini, <u>Nuclear Physics in Photographs</u>
 Oxford: Clarendon Press (1947)
- Smyth, H. D., Atomic Energy for Military Purposes

 Princeton, N. J.: Princeton University Press (1945)

B. Literature

- Bohr, N. and J. A. Wheeler, "The Mechanism of Nuclear Fission",

 Physical Review, 56, 382 (1939)
- Failla, G., "Biological Effects of Ionizing Radiations",

 Journal of Applied Physics, 12, 279 (1941)
- Fermi, E., "Elementary Theory of the Chain-Reacting Pile", Science, 105, 27 (1947)
- Grosse, A. V. et al, "Fission Due to U-235", Physical Review, 56, 382 (1939)
- Hamilton, J. G., "Metabolism of the Fission Products and the Heaviest Elements", Radiology, 49, 325 (1947)

B. Literature (Cont'd)

- Lapp, R. E., "Atomic Bomb Explosions Effects on an American City" *, Bulletin of Atomic Scientists, 4, 49 (1948)
- Lapp, R. E. and H. L. Andrews, "Health Physics",* Nucleonics, 2 (September 1948)
- Menke, J. R., "Nuclear Fission as a Source of Power", Econometrica, 15, 314 (1947)
- Morgan, K. Z., "Tolerance Concentrations of Radioactive Substances", <u>Journal of Physical and Colloid Chemistry</u>, <u>51</u>, 984 (1947)
- Seaborg, G. T., "The Transuranium Elements", Science, 104, 379 (1946)
- Seaborg, G. T., "Plutonium and the Other Transuranium Elements", Chemical and Engineering News, 25, 358 (1947)
- Stephenson, R. J., "A Brief Account of the Physics of the Atomic Bomb", American Journal of Physics, 14, 30 (1946)
- Turner, L. A., "Nuclear Fission", Review of Modern Physics, 12, 1 (1940)
- Way, K. and E. P. Wigner, "The Rate of Decay of Fission Products,"

 Physical Review, 73, 1318 (1948)
- Zinn, W. H. and L. Szilard, "Emission of Neutrons by Uranium",

 Physical Review, 56, 619 (1939)

^{*} Reprints available from Dr. R. E. Lapp, Research and Development Board, National Military Establishment, Washington, 25, D.C.

THE ATOMIC BOMB

AND THE

RESULTANT PHENOMENA

by

Dr. Herbert Scoville Jr.



THE ATOMIC BOMB

AND THE RESULTANT PHENOMENA

Dr. Herbert Scoville Jr.

The basic reaction in an atomic bomb explosion is the fission of either U-235 or plutonium. The various steps in this reaction can be shown by the following equation:

$$U-235 + n \longrightarrow U-236$$
 $\longrightarrow FP+FP+(1-3) n + V-rays$

In an atomic bomb this reaction is made to occur almost simultaneously on the part of a very large number of atoms. Since this reaction produces large amounts of energy (200 mev per fission) from the conversion of some of the mass of the original U-235, tremendous quantities of energy are released. This energy will be released in several different forms, i.e. as blast pressure, by the bomb explosion, optical or thermal radiation, and nuclear radiation. All explosive weapons produce high blast pressures and release some thermal radiation. Of all weapons yet devised, only the atomic bomb will release nuclear radiation. For this reason and not because it is necessarily of dominant importance, greatest emphasis in this discussion will be placed on the nuclear radiation, and the blast and thermal effects will only be mentioned for comparison with the nuclear radiation.

Types of Nuclear Radiation

Nuclear radiations produced from the detonation of an atomic bomb consist of a number of different types. First, and most important, are the gamma rays. Gamma radiation is high energy, electromagnetic radiation similar to visible light or x-rays. In fact, gamma rays have quite similar properties to x-rays, the only difference being that they have more energy and are consequently more penetrating.

When an atomic bomb is detonated, gamma rays are generated chiefly in two ways. First, prompt gamma rays are produced directly as a product of the fission reaction itself. Since the fission reaction is completed within a minute fraction of a second after the bomb is detonated, these prompt gamma rays are emitted practically instantaneously at the time of detonation. The second main source of gamma rays are the fission products themselves. In an atomic bomb explosion the fissionable material, uranium-235 or plutonium, splits into two atoms of intermediate atomic weight. Since the fission reaction does not always take place in exactly the same manner, many different elements are produced by fission in any atomic bomb detonation. These fission

products are almost all unstable and undergo radioactive decay emitting either or both gamma rays and beta particle.

The rate of decay of each of the various fission products is different, and the half-lives of the individual fission products will vary from fractions of a second to thousands of years. (The half-life of a radioactive material is the time required for half of the atoms of that material to undergo decay). Because of this variation in the half-life, gamma rays from fission products are smitted in decreasing quantities from the time of detonation to years later. As an approximation, it may be stated that the rate of decay is inversely proportional to the time after detonation. In practice this means that one hour after the detonation the radiation from fission products is 1/60 of that at one minute. Similarly, one day later the radiation is 1/24 of that at one hour, and one year later it is 1/365 that at one day.

In addition to the gamma radiation produced by an atomic bomb detonation, there are large quantities of neutrons emitted. A neutron, one of the elementary building blocks of all matter, is a neutral particle with an atomic mass of one. Because of their lack of charge, neutrons are extremely penetrating. Neutrons which have a very high energy, (i.e. fast neutrons) are produced as a direct product of the fission reaction. In addition, a smaller number of so-called delayed neutrons are emitted within a few seconds of the detonation as a product of the decay of a certain few fission products. The delayed neutrons also have high energies. Fast neutrons are slowed down by collision with molecules in the air so that at any appreciable distance from the detonation, both slow and fast neutrons are present. When neutrons are absorbed or "captured" by an atom of matter, they frequently make the matter artificially radioactive. This "induced" radioactivity is then often an additional source of gamma radiation.

As previously mentioned, the decaying fission products emit beta particles as well as gamma rays. These beta particles are high speed electrons which are produced in a nuclear reaction. Although the energy of these beta particles is high, their penetrating power is relatively low and would not produce appreciable effects more than a few meters from their source. They might, however, produce serious effects to personnel operating in an area contaminated with radioactive fission products. Beta emitting materials provide a serious hazard if absorbed internally.

Finally, a further type of nuclear radiation which may be present following an atomic bomb detonation is alpha particles. Any unfissioned plutonium or uranium-235 which may be present following a detonation will decay very slowly with the emission of alpha particles. The half-life of plutonium is 25,000 years and U-235 is 109 years so that the demission per unit time is greater for plutonium than for corresponding

amounts of U-235. Since alpha particles have little penetrating power and can be stopped even by a sheet of paper, they do not provide any external radiation hazard, but if an emitter gains entrance into the body either by inhalation, ingestion or through a wound, then the alpha activity might provide a serious hazard.

Detonation of An Atomic Bomb in the Air

Most of the atomic weapons which have been exploded to date were detonated in the air. The altitudes of these detonations have varied from close to the ground, in the case of the New Mexico tests, to high altitudes in the case of the two attacks on Japan. The information obtained from observations on personnel at Hiroshima and Nagasaki, and comfirmed by physical measurements made during tests, indicate that a median lethal exposure of gamma radiation is obtained in the open at a distance of about 3/4 to one mile from the point of detonation. Thus, most exposed personnel in an area of about two square miles would have been killed by these rays. However, the blast and thermal radiation throughout this same area would have been also very great so that a large number of casualties observed result from these causes rather than directly from the gamma rays. For comparison it is interesting to note that the blast damage to heavy concrete structures was extensive in Japan at distances greater than one mile from the point of detonation and residential structures were effected at distances greater than two miles. Exposed personnel were subjected to first degree burns at distances as far as two miles from the point of detonation, and serious flash burns were obtained at a distance of 3/4 of a mile. Protection against flash burns can, however, be relatively easily obtained since even thin coverings are sufficient to provide protection against this effect. Excellent examples of this are the photographs from Japan, which show severe scorching of exposed parts of the body as compared with relatively little effect on the skin, protected by light colored clothes which reflected the radiation.

The great penetrating power of gamma rays makes the problem of providing protection against them at close range extremely difficult. Experiments have indicated that about one inch of steel is required to reduce the gamma radiation by a factor of two. Concrete is about a third as effective as steel and ordinary dirt, about one-fifth as effective. Since, with an air burst, practically all of the effective gamma radiation is emitted almost instantaneously at the time of detonation, the source can be considered essentially as a point and therefore important shadow effects are produced by shield. However, since, at the distances where shielding is at all practicable, the radiation may be scattered several times, an important fraction of the total gamma radiation must be considered as coming from all directions. Therefore, although it is most important to have protection between the individual and the point

of detonation, it is necessary to have some shielding on all sides of the individual. This consideration is, of course, somewhat academic in practice since it will not ordinarily be possible to know in advance in what direction will be the point of detonation. It should be pointed out, in this respect, that since the largest fraction of the gamma rays are emitted instantaneously at the time of detonation, it will be impossible for an individual to take shelter from the radiation after he has seen the bomb explode. Personnel will only be safe if they are in dugouts, heavily constructed buildings, or large warships at the time the bomb explodes.

Although large quantities of neutrons are emitted at the time of the detonation of an atomic bomb, their range of effectiveness is in most cases negligible by comparison to that of the gamma rays. Nevertheless, because of the even greater penetrability of the fast neutrons, a situation could conceivably arise in which the gamma rays were absorbed and yet the neutrons penetrated and produced effects. However, in most practical situations the neutrons can be neglected. They might, however, induce radioactivity in certain elements near the point of detonation, and these might provide some residual radioactivity. This was the case in test Able at Bikini where the sodium in the sea water captured neutrons and became radioactive. While this interfered slightly with operations during the test at Bikini, it was probably not of sufficient magnitude to provide a serious problem in wartime operations.

The residual contamination both from deposited fission products and neutron induced radioactivity will depend on the altitude from which the bomb is detonated. Thus, at Alamagordo where the bomb was exploded close to the ground, the crater contained considerable amounts of residual radioactive material. Samples of material from this site are still radioactive. The size of this contaminated area, however, was quite limited. In Japan, where the bomb was detonated at much higher altitudes, there was little detectable radioactivity within a few days of the detonation.

Most of the fission products and unfissioned material in an air-burst are carried up to 30,000 to 60,000 feet in the atomic bomb cloud. These are then dispersed downwind and rapidly diluted so as to provide little hazard. However, there is a certain hazard downwind from a fall-out of this radioactive material, either as rain or as dust. For example, fifty miles away from the Trinity site in New Mexico radioactive materials fell on some cows and turned their hair white in spots. No other harmful effects were noted on these animals. Because of this danger it will always be desirable to track the cloud as it moves downwind, and survey areas which might possibly be contaminated by material falling out of it. However, in all probability, such fallout would be only a secondary hazard under wartime conditions.

Detonation of an Atomic Bomb Underwater

In an underwater detonation of an atomic bomb, such as occurred at Test Baker at Bikini, the effects are quite different from those which occur following an airburst. For example, with the one detonated at the depth used at Bikini, the thermal radiation effects were almost completely absent. The blast pressure produced by the explosion was evidenced in two forms, i. e., underwater shock and air blast. The air blast produced was not as great as that which occurs following an airburst, but was, nevertheless, very great and would have produced significant damage at some distance.

The nuclear radiation effects are also quite different in the two types of detonation, and would, in most cases, probably be more serious following an underwater shock than an airburst. The prompt gamma rays and neutrons are practically all absorbed by the water which surrounds the bomb. However, the radioactive fission products and unfissioned material are trapped in the water and carried aloft in the column and cloud. While the neutron activity induced in sea water may contribute to the total radioactivity carried aloft in this manner, it is nevertheless only a small fraction of the total. Thus the effects would be practically the same if the bomb were detonated in fresh or salt water. When the column descends, a concentrated mist shoots out from the base and spreads the radioactive materials over the surrounding area. The rain from this mist or so-called base surge and from the cloud will then deposit these materials leaving serious contamination over a large area.

The exact area covered by this mist and subsequently contaminated will depend on the wind velocity. As a rough approximation the lethal area may be considered to extend about one-half mile upwind and two or more miles downwind. Serious contamination would be obtained at a much greater distance. At Bikini nearly all the target ships, although otherwise undamaged, were heavily contaminated, and if the bomb were detonated offshore of some large city, the situation might well be catastrophic. In such a case a city might have suffered little visible damage and yet be essentially a ghost city. Most of the inhabitants at the time of the explosion would have been killed, evacuation would have been required for all others, and reentry of personnel would be restricted to limited periods. The effect of such an attack on a number of our large cities might completely paralyze the industrial power of our nation.

To give an idea of the magnitude of the problem it might be best to compare the radioactivity of the fission products with that of radium. A gram of radium is an extremely large quantity of this material and in fact only a few pounds had been isolated up to the beginning of

the war. In general one deals with thousandths or even millionths of a gram. The radioactivity from the fission products deposited in Bikini lagoon has, however, been estimated to be equivalent to thousands of tons of radium shortly after the detonation. This is a billion times the radioactivity from a gram of radium. Such is the truly fantastic radioactivity associated with an atomic bomb detonation.

Fission products deposited on the water would probably in most cases be diluted fairly rapidly, but would require tracking for appreciable periods of time. In the Bikini lagoon, which is a large body of water, intensities above tolerance were measured for almost a week, and even nontarget vessels operating in waters at sub-tolerance levels concentrated the radioactive material in their salt water lines and on their hulls in sufficient quantities to produce intensities above tolerances inside the vessels. This feature proved a great nuisance following the Baker test at Bikini, but would not have been sufficient to provide a serious hazard in wartime. However, had the concentrations in water been higher, then a serious hazard might have been produced. For example, at Pearl Harbor the volume of water is small and there is little exchange of water with the outside ocean. Under these conditions the water contamination might provide a serious problem.

Material deposited on solid surfaces such as the decks of the target ships or the streets of a city, downwind of such a detonation would be far more serious since it would not be subject to any diluting influences. The radioactive materials would be strongly absorbed and their removal would provide an extremely difficult problem. Decontamination of radioactive materials is quite different than for chemicals, for the former must be physically removed while the latter need only undergo some chemical reaction. As previously mentioned, the decay rate of a fission product mixture can be approximated by a 1/T law. Thus, the radiation from the contamination would at one month be about 1/30 that at the end of one day. However, if weathering could be neglected, another 30 months would be required before the radiation would be reduced by another factor of 30. Thus, it is obvious that any area which is still dangerous one month after the detonation will remain so for long periods of time. At Bikini half the target ships still had average topside radiation intensities greater than 1 roentgen per 24 hours two weeks after the test.

As time goes on, the danger from the external radiation, (i.e. exposure to gamma rays from a contaminated surface) will gradually become a secondary factor, and the internal radiation hazard will become of primary importance. Thus, long-life fission products and unfissioned material may be absorbed into the human system by inhalation of dust or by eating contaminated food stuffs. Under these conditions, beta and

alpha emitters provide the most serious radiation hazard. This type of hazard may well make large areas unfit for continuous occupation but it would not preclude the use of the area for temporary operations provided adequate precautionary measures were employed.

One further point requires mention with respect to the hazards from an underwater detonation. Unlike the airburst, the radiation exposure obtained following an underwater explosion is accumulated over a measured period of time after detonation. Thus, personnel in the open at a distance of one mile might have 30 seconds in which to take cover from the advancing radicactive mist. Direct exposure within this base surge would undoubtedly result in eventual death. Moreover unlike the airburst, the underwater detonation presents a hazard to any person entering the area sometime after the explosion has occurred. The extent of this hazard will, of course, depend on the time elapsed before such reentry is made. Thus if reentry into an area with an intensity of 3600 roentgens per 24 hours were made one hour after the detonation, then a lethal exposure of 400 r would be obtained in six hours and the dangerous exposure of 100 r in 20 minutes.

In order to understand some of the problems which are created by a possible underwater explosion, it is interesting to consider a hypothetical attack on one of our cities. First, the bomb, fitted with a fuse designed to fire at some later date, might be brought in peacetime by some innocent looking merchant vessel, deposited on the harbor bottom, and the ship could then retire without leaving any inkling of the impending disaster. At some later time the bomb would be detonated and we would have no sure knowledge even of whomour enemy might be. Thus, it might be feasible for some country apparently on good terms to carry out the disastrous attack with little fear of retaliation. Instead, our attack bombers might take off to drop their cargoes on some completely innocent country. The only method of avoiding such a situation is by alert intelligence. The need for competent intelligence services in this era of atomic warfare cannot be overemphasized.

An observer on the water front at the time the bomb was detonated might be suddenly surprised to see a tremendous mass of water shoot rapidly into the air and within a fraction of a second he would be knocked over by the air blast. If this, by chance, did not prove fatal, he would soon be engulfed in a driving rain and mist. This mist which is loaded with radioactive materials would expose him to a lethal amount of gamma radiation within a second after it reached him. For a mile inland of the water front the gamma rays from the radioactive rain and mist would probably be lethal to nearly all personnel. Few would have time to take adequate evasive action and all but a few who by chance happened to be in highly protected places would be doomed to eventual death.

Further downwind a variety of situations might occur. In some sections adequate alarm would not be received and these people would unknowingly receive serious and in many cases lethal exposures to the nuclear radiation. In other sectors the danger might be appreciated, but because of inadequate training and preparation, no effective evasive action would be taken. Instead, the people might mill around in the streets, panic stricken. Instead of an orderly evacuation they would, in many cases, move into highly contaminated areas and thereby increase their exposure. Thousands would be needlessly killed both by the nuclear radiation and by panic. The situation would be comparable to a fire in a theatre, except on an urban scale.

Where the advance preparation and training had been carried out effectively, the reduction in casualties might be considerable. Upon receipt of warning, the people should hastily descend to a basement and remain in an air tight room for as long as feasible. If the people can stay relatively well protected until the base surge has passed by, a tremendous reduction in the total exposure would be obtained. Moreover, the longer one can avoid venturing into a contaminated area, the smaller will be the exposure. As has been previously mentioned, the radioactivity decays very rapidly during the first few minutes or hours after the detonation. Thus, a person moving in a contaminated street five minutes after the detonation would receive more than twelve times the exposure of a person who could remain protected until one hour after the explosion.

Eventually, it will be necessary for all people to evacuate contaminated areas. If the planning has been adequate, this will be carried out in an orderly manner and with a minimum exposure to the radio-activity. This evacuation will be extremely difficult in certain cities. New York, for example, has few lines of exit and in the event of attack, many of these might be blocked off. It will be desirable for the people in charge of the evacuation to have, as rapidly as possible, an estimate of what localities are the most highly contaminated in order to avoid traversing them. One method of accomplishing this quickly will be by means of aircraft. Planes flying over a contaminated area at an altitude of 500 or 1,000 feet can make fairly good estimates of the degree of contamination at the surface. Such a survey could be made quite rapidly and would provide valuable information to rescue parties. A helicopter carrying a loud speaker could be used to direct people to uncontaminated areas.

Once the personnel have been evacuated from the danger areas, it will then be necessary to send in survey parties to determine the exact degree of contamination and what measures can be taken to rehabilitate the area. This will require large numbers of trained monitors. In addition, an adjacent command organization will have to be set up to correlate the results of the surveys made by the various individuals. Without such a command center, it will be virtually impossible to reenter

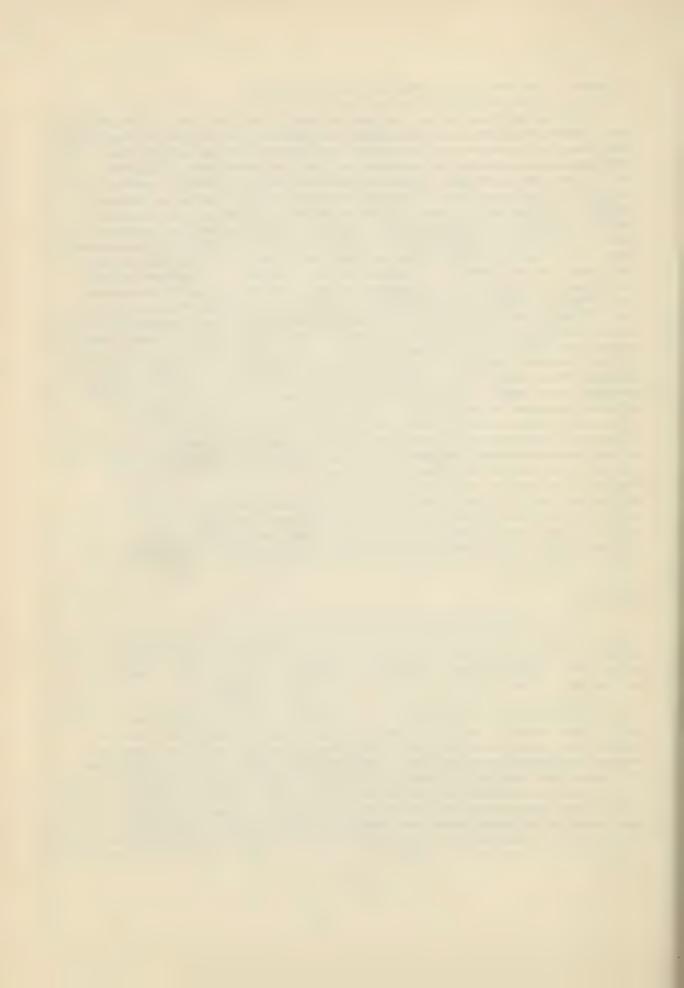
or rouse a city without extreme danger to personnel.

One point which should be kept in mind in all of these surveys and rescue operations is the large number of personnel which will be required. The areas to be covered will be large and the work of necessity slow. Moreover, the attrition in manpower may well be great even though no casualties are suffered. It is not intended to give here any precise value for a threshhold or minimum exposure which will begin to produce important biological effects, since sufficient information is not yet available on what this should be. However, for illustration purposes only, it might be assumed that this minimum exposure will be 50 roentgens. Thus, if a monitor in surveying an area, or a man in an area subjected to attack, accumulates 50 roentgens, he will be able to withdraw without suffering any ill effects. However, over a limited period of time there is little recovery or repair from an exposure to nuclear radiation so that it would be dangerous for him to receive any further exposure for a considerable period. Therefore, insofar as radiological defense operations are concerned, this man will be of no further use and he will have to be withdrawn insofar as possible from any danger of additional exposure. This using up of exposure will thus create a tremendous trained manpower attrition. Moreover, it will provide a serious administrative problem in order to keep track of the exposures of large numbers of personnel. This would probably be a medical responsibility, but in addition, it poses many difficulties for the commanding officer since he may have a company composed to ten men having had 50 roentgens and therefore unable to enter radioactive areas, 10 men with 25 roentgens who would be capable of limited operations, and others who could carry out normal radiological safety duties. Eventually it would probably be necessary to move all people who had 50 roentgens exposure into the socalled 50 roentgen company which would not be used in radiological defense operations. The same procedure would probably be followed for intermediately exposed personnel.

Summary

Airburst atomic bombs will produce lethal effects over an area of two square miles and measurable effects over an area of seven square miles as a result of the prompt gamma radiation emitted at the time of detonation. The residual radioactivity is of little importance except in the area close to the center of a low altitude explosion.

In an uderwater detonation, radioactive fission products and unfissioned material will be spread by the cloud and base surge over a large area. The gamma radiation from these materials will be lethal to exposed personnel more than two miles downwind, and serious contamination will result at even much greater distances. This contamination will provide a serious hazard for an indefinite period of time. Prompt and intelligent evasive action at the time of the detonation will permit the reduction of casualties, and orderly evacuation and reentry procedures will undoubtedly pay great dividends in minimizing the effects.



MEDICAL EFFECTS OF ATOMIC EXPLOSION

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Col. James P. Cooney



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Medical effects from the atomic bomb may roughly be divided into three categories as follows:

- 1. Trauma
- 2. Burns
- 3. Radiation Injury

l. Trauma - inflicted by the mechanical force of the explosion, either as blast or indirect trauma due to flying debris. As in the case of the bombing of Britain, the latter was much more important. The atomic bomb explosion differs from an ordinary bomb blast in the wide compass of its range. No one was closer to the bomb than several hundred meters. At that distance the peak pressure must already have fallen, and its duration must have greatly decreased in comparison with what it was in the center. The explosion did not have the trip hammer blow effect of high explosive, but was rather like a sudden violent gust of air which lasted for a brief but appreciable period.

Japanese medical observers on the spot could not find any cases of direct damage to the internal organs by the blast. Necropsy of the early cases shows no typical evidence of blast damage to the lungs. Many individuals reported having lost consciousness temporarily, with no history of direct trauma to the head. Observations of Zuckerman (British report) tend to discount cerebral concussion resulting directly from the blast. A report shows the total of 17 ruptured eardrums at Hiroshima and 22 at Nagasaki. According to the British investigators there is a great variation in the intensity of the blast pressure which will result in the rupture of the eardrums in man. In explosions where persons were subject to pressures estimated at between 45 and 100 pounds per square inch. less than onehalf of a small group suffered rupture of the tympanum. The drum may, however, rupture under pressures as low as two to four pounds in excess of atmosphere. Facts of acceleration of pressure may also be important in determining the incidence of blast effect on the biological target.

a. Indirect effects of blast caused by falling walls. flying glass, etc. Windows were broken as far away as Kure, 20 km. The radius of complete collapse of the wooden natives' buildings was 2.4 km, almost symmetrically distributed about the center. The incidence of mechanical injury is about 60% between 500 and 1250 meters. It is only beyond 2700 meters that the incidence of mechanical injury begins to fall off rapidly. Even at 4500 meters, the incidence of

mechanical injury in the survivor group is still 14%. Fatal injuries, however, are almost entirely in the zone of complete destruction.

Those indoors in heavy buildings, surprisingly, show a higher incidence of injury than those remaining in native Japanese buildings. Since most of the injuries were inflicted by flying glass and the concrete buildings have more glass than those of the native type, the explanation of the paradox is clear. Furthermore, this ratio of injury applies only to non-fatal injuries in survivors. It is assumed that the total mortality from immediate trauma is higher in the Japanese buildings than in the concrete buildings at the same distance, the reason being that over a wide area of impact the Japanese buildings collapsed from blast while the concrete buildings generally retained their structural integrity. Exactly how much of the total mortality was caused by the traumatic factor will never be known, because within onehalf hour following the blast both cities were swept by fire before rescue operations could be instituted. Consequently, even though mechanical injury was not directly responsible for death, it probably contributed vitally to the actual mortality. This accounts for the low incidence of severe forms of injury among the survivors.

The British estimate that a bomb similar to the one used at Nagasaki if exploded at the same height over a city such as London would cause complete collapse of normal buildings for a distance of 3,000 ft. from zero point, damage all houses beyond repair out to a distance of one mile, render houses uninhabitable without extensive repairs up to a distance of 1½ miles, and would render houses untenantable without immediate repairs out to a distance of 2½ miles.

Over London the bomb would completely wreck 30,000 houses, badly damage 35,000 and damage from 50,000 to 100,000. Based upon a density of population of one person per 1,000 sq. ft., the bomb would kill 75,000 people. Compare this with a 500 lb. bomb dropped in the same area which would cause a mortality of six people and a block buster which would cause a mortality of 30 people.

b. Types and mechanisms of injury from one group of patients at a military hospital were as follows:

Fractures 11.5% Contusions 53.8% Lacerations 34.7%

Flying glass was the cause of the greater percentage of lacerated wounds. The fragments were so small that in many cases clothing was sufficient to protect the body. In one

case at 1,000 meters, the patient was struck by glass fragments which, even though they did not penetrate his trousers, struck with sufficient force to pierce the skin of the upper portion of the bared torso and produce an injury.

2. Burns. The burns that occurred may be classified as "flash burns", which are the result of the direct action of radiant energy, and flame burns. The latter were relatively rare, for the reason that it took some time, perhaps one hour as stated above, for the fires that were started following the blast to spread within the city. Consequently, those who did not escape were burned to death.

The radiant energy covered the entire width of the spectrum, which resembled that of the sun. Let us now consider only the ultraviolet, visible light and infra red rays. None of these has a high degree of penetration, so that any solid object, such as clothing or even leaves, was sufficient to produce a shadowing effect (outline of the man who was in the direct line of rays projected upon the asphalt of Bantai Bridge), only surfaces directly exposed to the rays were effected by them and thus results the so-called "profile" burns. The wood of dark colored telephone poles was superficially carbonized at 3,000 meters from the center. From the data of Ashe and Roberts, a temperature of 4,000 degrees Centigrade acting for approximately 0.5 seconds is necessary to produce a second degree burn. It appears that the injurious agents causing flash burns were of extreme intensity but lasted for a very short duration. Burns were remarkably common among those indoors, as it was summer and many of the windows were open. Burns were of no significance beyond 4,000 meters. Beyond 3.000 meters few burns required treatment and were merely emphasized by erythema. Fifty-three percent of the deaths attributed to burns died within the first week and 75% of the total within two weeks.

Symptoms associated with the burns varied from case to case, but tended to follow a fairly definite pattern. In individuals close in, both burns and blisters were apparent in five minutes. Further out, in the vicinity of 1,500 meters, burns appeared in two hours time and the blisters in from four to six hours. Within 2,000 meters, the burns appeared in about three hours and blisters after an elapse of 10 hours. However, in one patient at 2,000 meters there was vesiculation within 10 minutes.

a. Effects of radiant energy upon the eye Direct injuries to the eye were remarkably few. Only a few palpebral burns were noted. The shadowing effects of the supraorbital ridges and the blink reflex helps to explain this finding. Almost all of the patients had temporary amblyopia which lasted for an average of five minutes. A few patients had conjunctivitis and kerititis. Only one patient with a

permanent scotoma from perforation of the macula was reported. Two patients developed traumatic cataract following contusions of the eyeball. A slight reduction in the transparency of the cornea was observed in some but they presented no subjective difficulties. One patient was so blinded by the flash that he was unable to distinguish light from dark for approximately two days but he made a complete recovery.

- b. Keloid Changes. Keloid changes appeared frequently and in many cases were extreme. According to the Japanese physicians, the incidence of keloids is not a characteristic of race and they attributed its large incidence to the extreme temperature. However, it has been noted that where skin flaps were removed for plastic surgery, healing resulted in keloid changes. A follow-up of the "keloid problem" is being made by the Atomic Bomb Casualty Commission.
- c. Pigmentation and Depigmentation. Among the striking features of burn were the changes in pigmentation. At a distance of approximately 2,000 meters beyond center, the pigmentation was extreme and resembled a walnut stain. (Mask of Hiroshima). These burns were preceded by an intense erythema, which within a few days became increasingly pigmented. Surrounding the hyper-pigmented area is a sharp border in which is found a zone where there is even less pigment than normal skin. This zone represents an area where some melanophores have abandoned to enter the hyper-pigmented tissue. This pigmentation began to fade only in a few cases at four months and in many cases still persists.

Depigmentation of the exposed skin occurred in distances less than 2,000 meters. It was not necessarily associated with the scarring of the skin. There is histological evidence that loss of pigment in the basal layers can occur, even though the epithelium of the surface is not destroyed. At the margins of the depigmentated zones there is found a narrow band of increased pigmentation externally to which there is again a vaguely defined depigmented border as described above. In the area of depigmentation, the erector pilorum muscles were not damaged.

d. Etiology of the burns. Certain features of the burns suggest the action of specific wave lengths, probably in the ultra-violet range. The intensity of the pigmentation at 2,000 meters and the extreme depigmentation without destruction of the skin closer to the bomb is certainly an unusual result of thermal injury, It must be remembered that a relatively small quantity of air intervened between the

patients and the bomb in comparison with the entire atmosphere and stratosphere which filters much of the ultra-violet from the sun. Gamma rays are not responsible for the sharply outlined pigmentary phenomena that has been described, since clothing would be no barrier to their action.

- e. Protective effect of clothing. Clothing exerted a protective effect depending upon a series of inter-related factors that include:
 - (1) Distance from the bomb
 - (2) Color and shade
 - (3) Tightness of the clothing
 - (4) Thickness and number of layers
 - (1) Distances. A khaki uniform, coat and shirt worn together, were protective beyond 1,500 meters. Closer to the bomb, clothes were no protection. In some instances clothing actually caught fire and the resultant flame burns were among the most severe that were encountered.
 - (2) Color and shade. Darker shades absorb more heat than lighter shades. The effect of selected absorption in many cases was remarkable. At 1,600 meters in the case of a white rayon shirt with a pattern of dark blue polka dots, 2mm in thickness and 1 cm apart, the polka dots were burned in the line of the rays but the intervening white material was undamaged. Extremely interesting is the effect upon cotton cloth with flower pattern in a light pink background. The flowers were dark red roses with leaves of varying shades of green. Some of the flowers were entirely burned out, others showing only scorching of the darker portions of the leaves and petals, while the intervening material showed no effects.
 - (3) <u>Tightness</u>. Where the clothing was more tightly stretched over the scapular and deltoid regions, burns were much more likely to occur.
 - (4) Thickness and number of layers. The protective effect of the seams and double layer effect of the folded over collar demonstrated the protective effect of the thickness of clothing.
- 3. Radiation Injury. The pathogenesis of the signs and symptoms will first be considered and then will follow an outline of the commonest clinical syndromes:

a. Skin. Epilation was frequently observed among persons who had been close to the bomb and who had survived for more than two weeks. At 500 meters the incidence was approximately 75% and fell off sharply at 1,250 meters. The time of the onset of epilation reached a very sharp peak between the 13th and 14th days after the bombing. Peak for males and females coincided. The hair suddenly began to fall out in bunches upon combing or general plucking, or it was found in considerable quantities on the pillow in the morning. This process continued for one or two weeks and then ceased. In most cases the distribution was that of an ordinary baldness, involving first the frontal and then the parietal and occipital regions, and sparing the temporal regions and the scruff of the neck. The eyebrows and even more so, the eyelashes and beard were relatively resistant. In one group of patients coming to autopsy, 48 had epilation of the head, 8 of the axilla. 6 of the pubic regions. 4 of the eyebrows and 2 of the beard. Complete epilation is not necessarily correlated with a bad prognosis. On the other hand, 14% of all individuals who died of radiation effect at approximately the fourth week had no epilation. It can be assumed that such cases received some shielding effect such as concrete buildings, thereby filtering out the softer rays, with death resulting from the hard penetrating rays which have little effect upon the skin.

Even in severe cases, the hair had begun to return by the middle of October and two or three months later had fully returned. In no case reported was epilation permanent.

- b. Oral and Gastro-intestinal Tissues. In many patients, severe nausea and vomiting occurred as early as 30 minutes following the detonation. In other cases, it did not occur until the next day. Thirty-two percent of the individuals within the first 1000 meters and 23% who were between 1100 and 1500 meters suffered from vomiting on the day of the bombing. The incidence fell sharply to 6% at 2000 meters. Diarrhea, sometimes sanguineous, occurred within the first few days in many patients. Lesions in the tongue, larnyx, esophagus and intestines which are the direct result of active radiation of such penetrating power, as to effect these deep mucous membranes more than the skin, occurred. Membranes, similar to the type found in agranulocytosis angina, occurred throughout the gastro-intestinal tract.
- c. Gonads. Histologically, radiation effects on the testes were discernible as early as the fourth day and were profound in all fatal cases who had been within 1500 meters of the bomb. It was obviously of interest to study the sperm counts in the survivors. Only three of the 23 patients studied who had been within 1500 meters had a count in excess of 40,000 (lower limit of normal); of 39 who had been with 2 km, 13 had counts below 40,000. According to

Macomber and Sanders, it is unusual for pregnancy to occur if the spermatozoa count is below 40,000. Several of the patients complained of a loss of libide or even loss of potency following the bombing. According to the Japanese physicians, the return to normalcy has been slower in the male than in the female.

- d. Ovaries. Histologically, the ovaries showed less striking changes than the testes. During the war years in Japan, there was a high incidence of amenorrhea, increasing from 4.3% in 1932 to 12.0% in 1944. In 1944 the incidence among 316 nurses of the Tokyo Imperial University was 13.3%. According to the Japanese gynecologists, this was due to malnutrition, overwork, and anxiety associated with bombing. Thirty-six percent of the women in Hiroshima and 29% of the women in Nagasaki, between the ages of 15 and 49, who were within a distance of 5000 meters experienced menstrual disorders. The majority of these had one normal period following the bomb and had cessation for an average of three to four months. A year later no cases complaining of menstrual disorders attributable to the bombing were found.
- e. Hemotopoietic System. In persons exposed to radiation, the lymphoid and hemotopoietic tissues underwent rapid necrobiosis. According to the Japanese, the effect on the blood was biphasic. The lymphocytes dropped immediately and reached their low point in about five days. A few days later the granulocytes began to drop and about the same time the lymphocytes began to recover. About the same time the reds began to fall and about the end of the third week, in many cases, there was a recovery of the lymphocytes with a marked decrease in granulocytes and an associated anemia. However, in some cases as early as five days following the bombing white blood counts as low as 150 cells per cubic millimeter were reported. Specimen of vertebral marrow obtained after 10 days following the bombing showed an almost total loss of myelopoietic tissue.
- f. Hemorrhagic Aspects. Involved in this are four factors, namely, platelet factor, dietary factor, infection factor, and capillary fragility factor.
 - (1) Platelet factor. In 14 cases dying between the fourth to seventh week, in whom platelet counts were available, only two were above 60,000 per cubic millimeters. Most of the cases ranged between 10,000 and 25,000. In all of these cases the bleeding time was increased, in some as long as 46 minutes.
 - (2) Dietary factor. Needless to say, vitamin C levels were low.

- (3) Infection factor. Specific bacteriological data was unsatisfactory. However, there were cases of bacteremia demonstrated by streptococci and bacilli found in freshly fixed tissues derived from the bone marrow.
- (4) Capillary fragility factor. Capillary fragility was found in individuals at the fifth week and at that time seemed to run parallel to the white blood count.
- g. Characteristics of the Hemorrhagic Phenomena. For convenience these will be referred to as purpura. In the skin, purpura was almost always manifested in patients dying from the third to sixth week, inclusive. Its incidence at various distances from the center ran almost exactly parallel to that of epilation and fell off sharply after 1250 meters. Purpuric spots tended to appear at about the same time as fever. Their peak is between the 16th and 22nd day, some five days later than the peak of epilation. The hemorrhages are most common in the upper half of the body and involve more particularly, the head, face, flexer surfaces of the upper arm, and the anterior aspect of the thorax. Associated with their onset, there is an increased tendency to bleed from lacerations. fractures and burns. Healing of wounds was prolonged, coincident with the appearance of radiation sickness. The growth of granulation tissue stopped and no tendency to heal was shown. In those who survived, the granulation tissue improved following recovery from radiation sickness associated with the purpuric spots on the skin. After the onset of the purpura of the skin, hemorrhages were also found in the gingivae and from the rectum, nose, urinary tract and respiratory passages in that order of frequency. The lungs are frequently involved in a necrotizing and hemorrhagic process.
- 4. Clinical Syndrome. Patients who dies of radiation sickness may be roughly divided into three groups as follows:
 - a. Patients who died within the first two weeks. In this group there is histological evidence of radiation effects upon the skin, gastro-intestinal tract, lymphoid tissue, bone marrow, gonads or ovaries, but these have not been clinically manifested. There was no epilation nor purpura. Patients complained of nausea and vomiting on the first day of the bombing, followed by anerexia, malaise, severe diarrhea, thirst and fever. Death ensued in delirium. Profound leukopenia was present. Temperature records in all these patients were remarkably similar. Usually between the fifth and seventh days and sometimes as early as the third

day there was a step-like rise in temperature, usually continuing to the day of death. The earlier the fever, the more severe the symptoms and the poorer the prognosis.

A typical case: A 31-year old petty officer of the Japanese Navy was admitted to the hospital the night of August 9th. He was within 250 meters at the time of the bombing and suffered first degree burns to the back, neck and chest, contusions of the nose and right hand and an abrasion of the left elbow. On the 12th of August he began to complain of abdominal pain, nausea, anorexia, dizziness and diarrhea, which reached a frequency of 15 stools a day. At the same time his temperature began to rise and gradually continue upward until the day of his death, 15 August 1945. His blood count on 12 August 1945 was 4.6 million red blood cells and 150 white blood cells.

b. Patients dying the third, fourth, fifth and sixth weeks or surviving severe symptoms. In this group, the anatomical and clinical results of radiation attained their acme. Epilation is prominent, as is the hypoplasin of the bone marrow. The hemorrhagic and necrotizing lesions are entirely comparable to those seen in aplastic anemia and agranulocytosis, and occur in the gums, respiratory and gastro-intestinal tract. Petechiae of the skin are almost always present. The sequence of symptoms is somewhat as follows:

In a typical severe case, the first evidence of the disease is nausea and vomiting on the day of the bombing, followed by a feeling of malaise. The patient then begins to improve and feels fairly well until about the beginning of the second week when epilation begins. A few days later he then again experiences malaise and a fever occurs, steplike in character. At approximately the same time pharyngeal pain may appear. Sanguineous diarrhea is a prominent symptom. The leucocytes and platelets reach very low levels and there may be an anemic and generally debilitated condition for a long period.

A typical case: A twenty-five year old soldier was at the 104th Garrison, approximately 1000 meters, on the upper floor of a two-story Japanese building at the time of the explosion. Fragments of glass struck his right arm and shoulder, inflicting a laceration on the former and contusion on the latter. That night he slept in a field but he returned to the garrison on the 7th. Between the 10th and 14th he worked on the east drill field and was able to march 15 km. Epilation began on the 20th of August but he continued

to work. On the 27th he felt feverish and on the next day petechiae occurred. He was admitted to the hospital on the 30th of August. At that time he complained of malaise, headache and swelling of the gums. He had previously had malaise on the day after the bombing. The gingivae continued to swell and on 4 September they were extremely painful. He had a sore throat on 1 September and had dysphagia on the 7th. Superficial ulcerations of the angles of the mouth were noted and on the next day he had trismus. temperature rose sharply on September 1 and attained 40.6 degrees Centigrade. On the next day it began to fall and reached normal levels on the 14th of September. Petechiae began to clear on 9 September and he was sufficiently well on 4 October to be discharged. He was next seen on 23 October by members of the Joint Commission who found him at work on his farm. At that time he complained only of shortness of breath. His white blood count reached 1400 in contrast with a low of 900 on 4 September.

c. In some individuals in whom the bone marrow fails to recover, the symptoms described in b above continue and the patients die after a chronic illness of extreme emaciation. In others, concomitant with partial or complete recovery of the marrow, most of the striking manifestations classed as anemia, disappear, but they nevertheless succumb to the complications such as lung abscess, tuberculosis, etc.

A typical case: A thirty-one year old man admitted to the hospital on 5 September 1945, complained of epilation, gingival pain and high fever. At the time of the bombing he was in the military barracks approximately one km from the center. At the time he sustained a large wound of the occipital region and lacerations of the upper arm and dersum of the left foot. On 25 August the scalp hair began to fall out and he began to complain of gingival pain. At the time of admission his temperature was 39.5 degrees Centigrade, pulse was 102. He was pale and undernourished and appeared moderately ill. There was a striking degree of gingival hemorrhage and ulcers were present on his lips. It was impossible for him to eat on account of pain. Epilation was complete but no petechiae were seen on the skin. On 15 September, his fever increased and his coughing was so severe that he was unable to sleep. However, his external wounds began to heal. On 14 November there was hemoptysis of approximately 100 cc. On 15 November he was in an agonal state and died. His total stay in the hospital was 72 days. On the 19th of September his red blood count was 2.2 millions, hemoglobin 36, and white blood count, 3200. On 8 November his red count had descended to 1.7 millions but his white blood count had increased to 4.300.

REFERENCES

General Report, Atomic Bomb Casualty Commission
January 1947

British Report on Hiroshima and Nagasaki

The Effects of Atomic Bombs on Hiroshima and Nagasaki, The United States Strategic Bombing Survey 30 June 1946



BIOLOGICAL EFFECTS OF RADIATION

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History

In 1895, while experimenting with cathode rays, Roentgen observed the fluorescence of some crystals lying at a distance from a Crookes-Hittorf tube. It was disclosed that a new ray had been discovered which was called an "x-ray". This discovery opened a new field of scientific and medical research and first brought ionizing radiation to the attention of mankind.

In 1896, natural radioactivity was discovered by Becquerel during a study of the fluorescent effects of various substances. While working with uranium, he found that photographic paper was darkened and, more important, that the air adjacent to the salts conducted electricity and discharged an electroscope. These phenomena indicated to him the presence of an inizing radiation, a radiation that was a specific property of uran um. In 1898 the Curies isolated the naturally radioactive elements polonium and radium from pitchblende.

It was soon after the discovery of the x-ray that the biological effects of radiation on skin were noted. This was the first indication of the biological hazards of radiation. Becquerel's classical accident was an example. After carrying a vial of radium in his vest pocket, he discovered a burn on the underlying skin.

During the next decade, radiation was used extensively as a therapeutic and diagnostic measure on almost every known disease and frequently with disastrous results. It was not until 1903-1905 that the marked sensivity of the blood-forming organs and reproductive organs of animals sounded the first warning that other than skin effects were occurring. Since that time the use of x-ray and radium has been approached with more caution as the dangers were recognized.

The above brief history has been pointed out to show that radiation is not a new problem introduced by atomic energy. However, the increased seriousness of the radiation problem because of the atomic energy industry and the more widespread use of radioactive material in the laboratory and in industry has stimulated more intense interest in studying the effects of radiation and especially the mechanism by which radiation produces biological effects.

Ionization

The damage or effect of radiation on tissue depends upon the absorption of the energy of the radiations by the biological material. The mechanism of this absorption is called "ionization", hence, "ionizing radiation". This mechanism consists of a radiation directly or indirectly striking an atom and dislodging an electron with the production of a positively charged atom and an electron, which are called "an ion pair". An atom which is in this state is capable of entering into abnormal chemical combinations or of breaking down or synthesizing complex molecules.

The different radiations produce ionization by different mechanisms. In brief, the charged particles, beta and alpha, act directly by applying their kinetic energy or electrical forces on the neutral atom and dislodge an orbital electron. Electromagnetic radiations (gamma, x-ray) and neutrons, ionize indirectly by accelerating a secondary charged particle which, in turn, produces the ionization. The gamma and x-ray photons strike free or lightly held electrons and impart all their energy to these secondary particles which, being accelerated, produce the ionization. process is known as the "photoelectric effect". There are two other methods by which photons produce ionization, but the results are essentially the same and in the interest of simplification, will not be discussed. Neutrons ionize primarily by colliding with nitrogen atoms with the release of a fast proton or by direct collision with hydrogen nuclei (proton); here as with gamma rays the accelerated secondary particle produces the ionization. All these radiations have in common the production of ion pairs. The ionization produced by any type of ray or particle is identical qualitatively, but quantitatively they vary as we will see later. But regardless of the quantitative effects of different radiations all radiation absorbed is damaging or of no value to the cell or tissue. One hears of stimulating doses of x-ray. Actually no such phenomena occurs and it is probable that the so-called stimulating effect is the response of the tissue to damage and is a mobilization of the body's protective mechanism.

Units of Radiation Measurement

The damage to tissue is due to the absorptions of energy from the radiation. At this time it is impossible to measure the exact amount of energy absorbed by the tissue, but it is assumed that the amount absorbed is proportional to the amount delivered within reasonable limits. In the measurement of radiation, the unit of quantity is the "roentgen" and it is defined as "The quantity of gamma or x-radiation such that associated corpuscular emissions per .001293 grams of air produce in air, ions carrying 1 ESU of electricity of either sign." This definition is a little

difficult to visualize. It can be said more simply to be the production of 1.6x1012 ion pairs per gram of air or 2x109 ion pairs per co of air or the absorption of 83 ergs per gram of air. The roentgen is a unit of absorption so a roentgen of different kinds of radiation will not represent the same energy flux as those of gamma or X-ray because of difference in wave length or absorption coefficient. Thus roentgen equivalents have been developed which will allow comparisons. One is the "rep" which is that amount of radiation which produces energy absorptions of 83 ergs per cc of tissue. A second is the "rem" which is that amount of radiation which produces a biological effect equal to that produced by 1 r of high voltage X-ray (400 kv). The use of the latter unit will permit additive radiation doses within limits.

The following is a comparative scale of the various units and types of radiations.

X-rays and gamma rays 1 r = 1 rep = 1 rem

Beta rays - 1 rep = 1 rem

Protons and fast neutrons - 1 rep = 4 rems

Slow neutrons - 1 rep = 4 rems

Alpha particles - 1 rep = 10 rems

Specific Ionization

As can be seen from the above chart, the biological effectiveness as indicated by the rem, varies with the type of radiation. As previously stated, the biological effect is due to the absorption of energy, and the energy absorption is manifest by the ionization in the biological material. "Specific ionization" is the term used to indicate the relative ability of a radiation to produce ionization in a short distance and is defined as the number of ion pairs produced directly or indirectly per unit length of the ionization tracks. In general, the biological effectiveness increases with the increase in specific ionization since more energy is absorbed per unit of tissue. This accounts for the statement that the effects of different types of radiation are qualitatively indistinguishable but differ in their quantitative results. A general rule that may be followed is: along the track of an individual particle, the specific ionization varies directly with the square of the particle charge and inversely with its speed. On this basis, alpha with its two charges is more effective than a proton or an electron. Also an electron of high energy would be less effective than one of lower energy or less speed in producing specific ionization. When the electromagnetic radiations are considered, their biological effectiveness varies with their energy and the energy imparted to the secondary electron which produces the ionization.

This is based on the theory of multiple hits or several ionizing events in the same cell being required to produce biological effects. The probability of a radiation with ionizing events scattered throughout a long track producing a demonstrable effect is less than one concentrating its energies in a small unit of tissue. To illustrate, the following dosage in roentgen units was required to kill mice within three weeks after whole body radiation.

Gamma 2 mev 675r

X-ray 200 kv 500r

Fast neutrons 225 rep (90n)

The figures given for the specific ionization of a particle usually represent the average specific ionization as the amount of ionization changes along a track as the speed decreases, which follows the general rule given above.

Internal and External Radiation

There are two general methods of exposure to radiation which must be differentiated, i.e. external and internal.

External. Here the source of radiation is located outside the body and the radiation must pass into the skin and into the deep tissue, depending upon the type of radiation to produce effects. With an external source, radiation effect may be stopped by removing the source, moving away from the source, or by interposing adequate shielding between the body and the source.

Internal. In this case the source of radiation is taken into the body in ingestion, inhalation or through a break in the skin. The fission products or other radioactive elements are then deposited in the various organs of the body, the most important being a deposition in the bones in close proximity to the bone marrow. When radioactive material is fixed in the tissue, it is often excreted very slowly and so remains a long term source of radiation bombardment within the individual. There is no known process to destroy or neutralize the radiation source, and methods to speed the excretion or cover the fixed material are unsatisfactory. The only limiting factor, other than excretion, is the normal decay rate of the radioactive element.

It might be well to mention at this time other units which occur in the literature and in any discussion of internal hazards. The physicists have defined for you the half-life of a radioactive element as the time required for one half the elements to decay. In biology and medicine we have two other units: (a) "biological half-life" - the time required for one half of the material to be excreted, and (b) "effective half-life" - the time required to lose one half the material by a combination of excretion and radioactive decay.

Tolerances or Maximum Permissible Dose

Past experience in using x-ray and radium for diagnosis and therapy and laboratory experience in radiation has developed levels of radiation which at least tentatively are considered safe to absorb over a long period. This has been set at .1r of 100 mr/24 hrs of gamma or an equivalent amount of the other radiations. The rate at which it is absorbed within the daily permissible dose is immaterial. The rate of absorption is important, however, when considering higher dosage, as you will see later. In all industrial processes, an effort is made to stay within this tolerance figure. At the present time reduction in the permissible dose is being comsidered, especially for women workers, due to the greater susceptibility of the female uterus and ovaries to radiation injury as evidences in animal experimentation. The 100 mr/24 hrs is a permissible dose, not a dose that is desired nor one that should be taken unnecessarily. No more radiation should be absorbed than is required for the job.

The above tolerance is established as an industrial and peacetime value. We of the military, however, must keep in mind that in
the event of war, most values change and specifically we must expect
that military and defense personnel will be called upon by necessity
to exceed the peacetime tolerance value. Individuals are injured in
war by the conventional weapons while doing the job that is required,
and it must be expected in respect to radiation that a military
tolerance must be developed and accepted as one of the risks of warfare. This value must be set at a level short of acute radiation
illness so that the majority of the individuals will be able to
complete their job or mission and at a comparable risk to that
commonly accepted by field commanders working under the hazards of
conventional weapons.

With regard to internal radiation in peacetime or in industry, the goal is no absorption of radioactive material Tolerance levels in internal radiation are more difficult to determine because of variable biological factors such as absorption and excretion and the difficulty in measuring the amounts actually fixed in the tissues, and also the lack of actual toxicity experience or figures in man. Experimental work with these materials must necessarily be done with animals and the translation into values for man is questionable. The notable exception is radium as the result of the historical radium dial posioning cases. The maximum allowable figure for radium fixed in the tissue is .1 microgram. Another element, plutonium, has been widely used in the atomic energy industry and sufficient work has been done to establish the value of 1 microgram as the limit of tolerance.

Lethal Dose. The lethal dose of external radiation is fairly well established and current thinking places the median lethal dose, the dose at which 50% deaths would be expected, at 400 to 450 r or roentgen equivalents and the 100% lethal dose at approximately 700 to 800 r. It must be remembered that when we speak of doses of hundreds of roentgens being lethal or causing serious physical damage, we are speaking of irradiation of the entire body or whole body radiation. Doses up to thousands of roentgens may be given to a small confined area of the body without causing serious injury except to the desired area.

Observed Biological Effect in the Cell

The damage which results through the action of radiation on tissue takes place in the cell or in its immediate environment. The actual mechanism by which this ionizing energy causes injury is still unknown. Several mechanisms have been advanced and among them are:

- 1. Some chemical exchange which interferes with the normal interchange between the nucleus and the rest of the cell
- 2. Changes in permeability of the cell membrane
- 3. Production of a toxic substance in the cell
- 4. Changes in the intercellular environment.

Intensive work is being done in the experimental laboratories in an effort to solve this problem.

After the damage to the cell has occurred, some effects can be directly observed by microscopic techniques such as:

Chromosome breaks
Clumping of the chromatin
Changes in cell division with formation of giant cells
or abnormal mitosis
Increased granularity of cytoplasm
Changes in affinity for various stains
Changes in motility or function of cell
Cytolysis
Swelling of the nucleus or of the entire cell

Less direct physical methods reveal other effects, such as changes in the viscosity of the protoplasm, or in the permeability of the cell membrane. It seems probable that only a small fraction of the cellular effects produced have yet been observed, and it must be mentioned that the above observable effects can result from other stimuli besides radiation and a specific radiation effect does not exist.

Factors Involving Radiation Effects on Biological Material

Celiular Response. A cell is made up of several distinguishable parts which differ in chemical makeup. As radiation passes through or into the cell, all these parts are radiated simultaneously at random and it is not surprising that many effects can be observed in the same cell or groups of similar cells following the same dose of radiation. When many-celled organisms are radiated, the complexities are increased by the variation in response of individual cells of the same type and of cells of different types, and the possibility that in multicelled organisms, radiation damage to one tissue may produce indirect effects on others.

Cellular Environment. Changes or alterations in the cellular environment may be a direct or indirect factor determining the observed cellular damage due to ionizing radiation. It is known that changes in environment will alter the radiosensitivity of the tissue. Cold-freezing and anoxemia will decrease the radiosensitivity. Changes in the acid base relationship which effect the osmosis of the cell membrane will in certain tissues, increase their radiosensitivity.

Sensitivity of Tissue. Radiosensitivity of the tissue means the relative vulnerability of the tissue in its normal state to ionizing radiation. This sensitivity within limits is predictable for different types of tissue under the same conditions of exposure. A general rule can be given that is useful as a rough guide; less highly specialized tissue (white blood corpuscles and reproductive cells) are more sensitive than the highly specialized tissues (brain, nerve cells). Further, the rapidly multiplying or actively reproducing tissues are more sensitive than those in a more quiescent state. This is partially the basis for use of radiation in the treatment of new growths or malignancies. The tumor suffers greater radiation damage than the surrounding normal tissue. Without detail, the following may be accepted as a list of the common tissues in order of their decreasing radiosensitivity:

Lymphoid tissue, bone marrow, blood

lymphocytes, lymph nodes, peyers patches
Polymorphonuclear leukocytes
Epithelial cells
Gonads and ovaries
Salivary glands
Skin and mucous membrane
Endothelial cells - blood vessels and peritoneum
Connective tissue cells
Muscle cells
Nerve cells

Species Sensitivity. Che of the peculiarities of radiation is the wide variation in response of different species to identical doses of radiation delivered under the same conditions. An example of the variation can be seen in the different values of the median lethal dose for animals exposed to 200 kv x-ray: mice, 500r; guinea pigs, 250r; rabbits, 875r. This specie difference is troublesome since by necessity we must use animals in the exploration of radiation effects, and it is not always possible to apply the results, other than qualitatively, to man. As in all biological work, and especially so in radiation because of the variation in response even within a specie, it is impossible to measure effects of a single specimen but all results must be measured by statistical methods.

Intensity of Radiation. Another factor which must be considered in discussing the biological effects of radiation is the influence of rate of delivery on the final results. It can be summarized in three categories:

- a. Many effects are produced independent of the rate of delivery of the radiation. These are the so-called cumulative or additive effects. The total dose is the important value. Among these are genetic effects and the influence of radiation on the development of uterine tumors in mice.
- b. In a few instances it has been reported that the effectiveness of radiation has been increased by the decrease in rate of delivery. This is explained on the basis of an increase in radiosensitivity of tissue under prolonged radiation.
- c. In most instances, biological effectiveness of a given dose decreases as the rate of exposure decreases. This is explained by the theory that the radiosensitivity of the tissue decreases under prolonged radiation, but it is more easily explained by assuming a recovery factor of the tissue. If, however, the intensity or rate of delivery is increased, recovery falls behind the damage and an increase in effectiveness of a dose is apparent. It is this recovery factor or decreased effectiveness of low intensity exposures which is important to industrial workers suffering daily exposure. If all effects were cumulative, it would be impossible to operate under such a low tolerance value as 100 mr/24 hrs.

Reversibility of Effects. Tissue which has been damaged by radiation follows the same general rules as tissue damage by other stimuli. Those tissues which are incapable of reproducing functional cells after destruction will not recover from radiation damage

except by the formation of scar, i.e. muscle, brain and portions of the kidney and eye. Those which normally regenerate functional cells will recover. This, of course, is dependent on the total amount of radiation absorbed, there being a level of damage in all tissues at which recovery is impossible and tissue is replaced with scar. It must be remembered that tissues receiving repeated damage by radiation may not recover. If extensive damage has been done to a tissue by radiation, a repetition of this injury must be avoided if a functional result is to be obtained or if the possibility of malignancy is to be eliminated.

Distribution and Penetration of Radiation. In all our discussions on the effects of the atomic bomb, we are speaking in terms of whole body radiation and not localized radiation as is used in therapy.

We have already discussed the biological effectiveness or specific ionization of the various rays and particles. Penetration of the radiation must be considered in evaluating the biological hazard. To produce their effects, regardless of their ionizing ability, they must reach tissues which can be damaged. Alpha particles (heavy charged particles) are highly ionizing, but their range of action is limited by their poor penetration in tissue (approximately .1 mm). This practically eliminates alpha particles as an external hazard as they may be shielded with a few pieces of paper or the squamous portion of the skin. It is only when they are deposited internally in vulnerable organs such as the bones that severe damage due to the highly ionizing ability becomes apparent. Beta particles have a similarly poor penetration quality (approximately 5 to 10 mm in tissue) so may be rated as an internal radiation hazard. However, they do have a strong caustic effect on the skin at short distances so must also be considered as an external hazard. High energy gamma rays and x-rays have a much less degree of ionization than alpha particles, but their ability to penetrate and reach the deep tissues makes them the major external radiation hazard. The penetrating ability of neutrons is somewhat less than that of gamma and their ability to ionize is from 5 to 10 times as effective as gamma so they may be classified as a serious external hazard.

Acute and Chronic Radiation.

Acute radiation injury must be separated from chronic in any discussion of radiation hazards. The acute results from dosage producing an effect that can be determined by clinical and laboratory examination. It results from doses approaching 100 r. Acute radiation sickness is a clinical entity which will not be discussed in this lecture. Chronic effects resulting from dosages ranging

from so-called tolerance levels to approximately 10 to 20 r per day are the subject of intensive research but little data on man is available. The results of animal experimentation must suffice because of the unsuitability of exposing humans to this hazard. The predominant effects expected of chronic radiation are shortening of the life span, premature aging, production of malignancies, skin changes from beta and soft gamma and x-ray, and genetic injury. It must be remembered that the above effects are the result of repeated and prolonged radiation, not to be expected from occasional exposure over the tolerance dose. Most of the evidence now available on these injuries has been obtained from injuries of radiologists and industrial x-ray workers. It is worth repeating again that the chronic effects of radiation are due to prolonged or repeated insults to the tissue and not occasional mild or moderate overexposures.

Blood Changes.

The blood is a factor mentioned as an index of radiation exposure. This is in line with the high radiosensitivity of lymphoid tissues and the bone marrow. Off hand, one would assume that observations of the blood count and injury to the blood forming tissues should reflect radiation damage. This is true for severe overexposure. Alteration of the blood picture may be observed a few hours after overexposure to whole body radiation. This alteration is seen as a reduction in the white blood cells and in very severe overexposure, a reduction in the red count. However, in low grade overexposures or those exposures in the neighborhood of the tolerance value, the blood count is not a reliable index when considered independently. The daily normal variations, existance of unobserved low grade infections, and variations in counting technique are among the factors reducing its reliability in measuring the relative small variations to be expected. A count on an individual exposed to frequent radiation showing a reduction, even when compared to the individual's previously established normal, is not a positive indication of radiation injury and must be evaluated with other physical factors. Importance can be attached to the reduction only if the individual is a member of a group exposed to the same radiations and all show the same variation. That would possibly indicate an overtolerance exposure to radiation for the group.

Reproductive Organs.

The elements of the reproductive organs which are injured by radiation are the progenerators of the adult germ cell. High intensities of radiation or prolonged radiation will cause a complete destruction of the germ cell producing tissue. Permanent sterility can be produced in the male with a dosage in the neighborhood of 800 r and in the female of 600 r. Temporary sterility is produced

at lower doses and as for the Japanese casualties who survived large doses of whole body radiation and were sterile, the majority have recovered. It is somewhat of a paradox that among the female casualties a higher percentage has recovered and at a faster rate than the male. The differences between sterility and impotence must always be kept in mind when speaking to the laymen about radiation effects or more specifically, effects from the atomic bomb. Confusion does exist in their minds and they can be assured that impotence is not a result of radiation and is a separate and distinct entity from sterility.

Genetic Injury

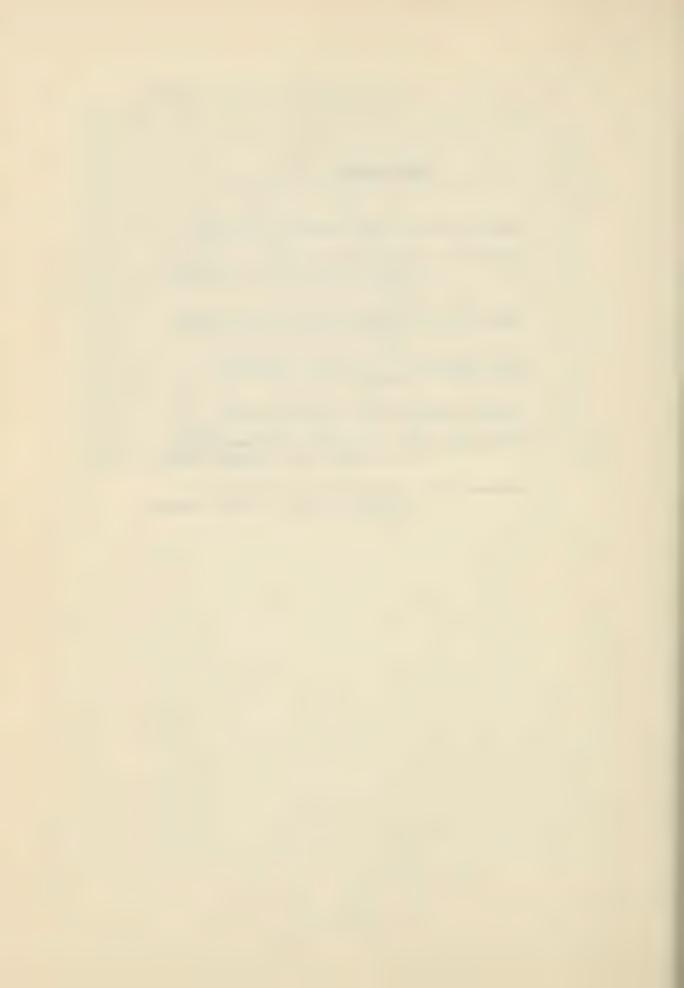
Genetics is a complicated and somewhat obscure science rarely considered by the average medical man. In radiation, however, it is constantly mentioned as a hazard and no discussion of radiation injury is complete without the mention of genetic injury. A factor which probably causes the most concern is that accumulative dosage without regard to rate or energy produces the effects. Further, it is thought that only one ionizing event is sufficient to cause a change in the gene rather than multiple hits or several ionizations as is considered necessary to produce the majority of the biological effects. Little is known of the actual effects to be expected in man because of his long life span, small number of offspring, and the difficulty of controlling long-term experiments. The information most quoted has resulted from studying the fruit fly and various species of fish. Thirty or 40r is sufficient in the fruit fly to produce demonstrable increases in mutation rates. Approximately 500 r are required to produce similar changes in mice and it is estimated that 600 r would be required to produce significant changes in the mutation rate in man.

The gene is a germinal factor present in the chromosomes which carry the hereditery characteristics. There are two types, the dominant and the recessive. The recessive requires a like gene or a like contribution from both parents for expression in the offspring. A dominant gene will be expressed in the direct offspring regardless of the other parent. Mutations are the changes in the characteristics of a gene. It is these mutations that produce abnormalities in the offspring which may be either deleterious or beneficial to the race. They occur naturally and under artificial stimulation. Radiation will produce mutations. As stated before, mutations in dominant genes may be detected in the next generation while those in recessive genes may go undetected for generations. Fortunately, the majority of the natural and artificial mutations are recessive and require a similarly abnormal gene for expression. The one exception to the general rule of recessive requiring a like recessive for expression is the sex linked genes carried by the female sex cell. Because the male does not carry a similar gene, they act as a dominant and abnormalities in that gene will be apparent in the next generation.

Mutations in man, whether spontaneous or artificial, are about 95% lethal or sublethal which means that the offspring will die during gestation or shortly afterwards. Of the viable mutations (5% of all mutations) about 95% are deleterious. Of these, about 96% pertain to other than sex chromosomes. The subject of genetic changes and the production of a race of monsters in Japan as the result of the atomic bombings has received a large amount of publicity in this country. Actually, no such disaster is possible or contemplated by geneticists. The National Research Council and the Atomic Emergy Commission, through an organization called the Atomic Bomb Casualty Commission, are running a long-term study in Japan to determine if possible any evidence of genetic changes. The fact of survival indicates that probably less than 400 r had been absorbed which is considered too low a dosage for genetic changes to appear in man except for the changes which may appear in the sex linked genes in females or those that appear with lower doses in any statistically measured effect. Ordinarily, more males are born than females and in Japan they expect possibly to find an increase in the male mortality rate and as a result, a change in the male-female ratio to approximately 1 to 1 or possibly a slight increase in the number of females. The number of survivors in the reproducing age group which were in that border line zone of high dosage but survived, is relatively small when considered against the total population of their city and would be productive of low demonstrable genetic changes.

BIBLIOGRAPHY

- Zirkle, R. E. Lectures, Argonne Laboratory
- Cantrell, S. T., Biological Effects of Radiation in relation to Occupational Exposure
- Fuqua, P. A., Lecture, Effects of Radiation On the Body
- Gamertsfelder, C. C., Lecture, Radiation Dosimetry
- Parker, H. M., Lecture, Tolerance Dose
- Lapp, R. E. and E. L. Andrews, "Nuclear Radiation Physics" Prentice-Hall 1948
- Lorenz, Hestor, Eschenbrenner & Deringer Biological Studies in the Tolerance
 Range



ESSENTIALS OF INSTRUMENTATION

by

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ESSENTIALS OF INSTRUMENTATION

Dr. Howard Andrews

The detection and measurement of high energy radiation depends entirely upon the proper use of suitably constructed instruments since nature has not seen fit to provide man with senses capable of responding to it. Without instruments even intense radiation fields will not be recognized until irreparable damage has been done. If photographic film and a few special methods are excepted, all detecting devices are based upon the ionization produced in gases by the incident radiation. When an ionizing agent enters a gas, it may act on a neutral atom or molecule with a force large enough to remove one or more electrons from the atom. It is most probable that two ions will be formed, and so it is customary to speak of the formation of ion pairs. The average energy loss per ion pair in air is about 33 electron volts.

If ions are formed in a gas subject to an electric field, they will move in opposite directions, the negative ions toward the positively charged anode and the positives toward the negatively charged cathode. The current flow will be extremely small, and special measuring devices are required to detect it. Because of the mutual attraction of oppositely charged particles there is always a tendency for ions to recombine and form neutral atoms. The chance of recombination is greater the longer the time before the ions reach the electrodes. The fraction lost decreases with increasing voltage, and eventually all of the ions are collected so there is no further increase in current. This condition is known as saturation, and the maximum current is called the saturation current.

Instruments for measuring the amount of electric charge collected in an ionization chamber are known as electroscopes and electrometers. The <u>Lauritsen electroscope</u> is one of the most generally useful instruments for radiation measurements. The moving system is a quartz fiber about 5 microns in diameter, made conducting with a thin metal coating and cemented to one arm of an L. Mutual repulsion causes the quartz fiber to deflect. Ions formed inside the case will neutralize the charge and the fiber will return toward its uncharged position.

Another useful quartz fiber instrument is the pencil type electroscope, or dosimeter. This is essentially a Lauritsen electroscope modified so that the entire instrument is about the size of a large fountain pen. Instruments of this type are very useful for measuring integrated exposures. They can be made with a sensitivity such that 0.1 roentgen will produce about one half of full scale deflection.

Ionization chamber instruments vary widely depending on the particular type of radiation to be detected. Short range radiation is admitted to the chamber through a suitable window. Thin mica or stretched nylon film about 0.000l inch thick is satisfactory for alpha particles. If beta particles are to be measured, the windows need not be so thin. When a photon enters the ion chamber and is absorbed, high speed electrons are produced which travel through the gas in the chamber producing ions until their kinetic energy is spent. For 0.2 Mev X-rays this requires a chamber about 20 centimeters in diameter.

A small portable chamber should have the same absorption for X- and gamma rays as the air in the standard chamber and should also have the equivalent of the long air paths for the absorption of the high energy electrons. Chamber walls are regularly made of bakelite or plastics which contain a high percentage of carbon atoms. Since human tissue is composed chiefly of carbon, oxygen, nitrogen, and hydrogen, such an instrument will simulate absorption by the body. Ionization chambers designed on these considerations are known as thimble chambers. One successful thimble chamber instrument is the condenser gamma meter.

The condenser gamma meter is not entirely satisfactory for survey purposes. The chambers must be charged, left in the radiation field for an appropriate time, and then read with the meter. If a large contaminated area is to be surveyed, the number of chambers required becomes exorbitant. This requires an instrument which will give a steady deflection that is proportional to the amount of radiation striking the chamber. Unfortunately ionization currents are too small to be measured with portable meters, and it is necessary to use other means. It is perfectly feasible to measure currents of this order with suitable vacuum tube circuits.

Geiger-Mueller (G-M) counters take advantage of the gas amplification that can be obtained when high accelerating voltages are applied to an ionization chamber. When an ion has an energy greater than the ionization energy of the gas molecule, it may produce secondary ions upon collision. The secondary ions formed will in turn be accelerated by the electric field and may produce further ionization. This cumulative effect is known as Townsend or avalanche ionization. If a total of A ion pairs results from one original pair, the process is said to have a gas amplification factor of A. In practice A varies from about 10 in gas-filled photoelectric cells to 10° in some Geiger-Mueller counter tubes. At a pressure of 10 centimeters of mercury, gas amplification can be obtained at voltages of 250-1, 500 volts depending on the gas and the tube dimensions. G-M counters usually have a cylindrical cathode from 1 to 10 centimeters

in diameter with a length from 2 to 10 times the diameter. The anode consists typically of an insulated axial wire 0.0001-inch to 0.0005-inch in diameter.

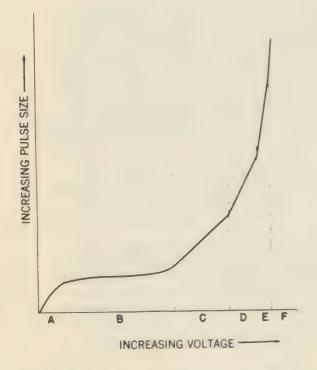
Assume such a counter exposed to a constant amount of radiation. each ionizing particle or photon having the same energy, each ionizing particle entering the chamber will produce a definite number of ion pairs in the gas, and these ions will proceed to the collecting electrodes where they will be neutralized and will produce a pulse of current in the external ciruit. If now the size of the pulse is plotted against the voltage applied to the electrodes, a curve similar to that of figure 1 will be obtained. Regions A and B represent the normal ionization chamber working conditions where the only ions contributing to the pulse are those produced by the original radiation. Over region C there is some gas amplification occurring very close to the central wire. In this region the gaseous amplification is quite stable for any given voltage and does not depend on the number of initial ions present. Thus if the voltage is adjusted to a value such that the gas amplification factor is 103 and an incident beta particle produces 100 ion pairs, the pulse received at the electrode will be 100X103=105 ions. Under the same voltage conditions an alpha particle producing 105 primary ion pairs will yield a pulse of 105X103=108 ions. Because of the rather strict proportionality between the amounts of initial and total ionization this portion of the curve is known as the region of proportionality, and a counting tube operating in this region is called a proportional counter. A proportional counter can be used to measure alpha particles or neutrons in the presence of strong beta and gamma radiation.

If the voltage is raised still further, the gas amplification factor will continue to increase, but in region D the amplified pulses are no longer proportional to the number of primary ions. A sort of saturation effect begins to enter at this point and consequently a few primary ions will produce nearly as many total ions as are obtained from a large number of primaries. There is still some difference in final pulse sizes however, so this region is known as the region of limited proportionality.

The gas amplification continues to increase with further increases in voltage, and region D gradually changes to region E where all proportionality ceases. Here a single ion pair is sufficient to produce an amplified pulse of the same size as that obtained from a large number of primary ions. This is known as the Geiger region and is characterized by gas amplification factors of the order of 108. This is the portion of the tube characteristic commonly used for counting beta and gamma radiation. The Geiger region usually extends over a range of about 200 volts. When still higher voltages are used, the region of continuous discharge, F, is reached. In this region the tube is too unstable for useful operation, and care must always be taken to keep the tube voltages below the continuous discharge value. Actually the tube does not go into continuous discharge but rather

produces a series of closely spaced pulses from one initial ionizing event.

A second type of characteristic curve is helpful in understanding the operation in the Geiger region. Assume the tube to be exposed to a constant radiation intensity but with the incident particles or photons having unequal energies. Pulses per second when plotted against the applied voltage yield a curve similar to figure 2.



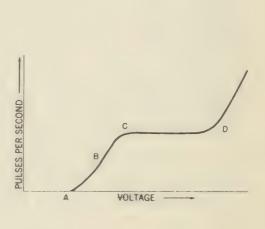


Figure 1 - Ion chamber pulse size versus voltage.

Figure 2 - G-M tube characteristics

The associated electronic equipment for recording the number of pulses will not respond to the small pulses produced in the ionization chamber region where there is no gas amplification. Consequently the curve will have a threshold, A, below which no pulses will be recorded. As the voltage is raised and the gas amplification becomes appreciable, the most energetic particles will be counted, but the weak ones will be lost. This is the region of proportional counting AB. As the gas amplification continues to increase with

voltage, more of the less energetic particles will be counted until point C is reached. C is the threshold of the Geiger region, CD, and here practically every particle entering the tube is counted. D is the threshold of the continuous discharge region.

The Geiger region CD is known as the plateau, and it is obviously desirable for a tube to have a long, flat plateau since here the counting rate does not depend strongly on the applied voltage. To obtain desirable plateau characteristics the filling gas and pressure must be carefully chosen, and the central wire must be free from dust, sharp points or diemarks. Oxygen and water vapor are particularly undesirable and must be completely removed before filling. Argon is a very satisfactory gas and is used in practically all counters.

Near the central wire a large number of electrons and positive ions will be formed in the avalanche. The electrons have a small mass and are already close to the central wire so they will move toward it with high velocities and will be completely collected by the wire in 10^{-6} seconds or less. The positive ions, on the other hand, have to travel out of the negatively charged cylinder. Since they have comparatively large masses, they move much slower than the electrons. The positive ion cloud will reach the cylinder in perhaps 10^{-3} seconds, long after the electrons have been collected at the wire.

As a positive ion approaches very close to the cylinder, it will pull an electron from the cylinder and become a neutral molecule. In general the electron will go into one of the upper energy levels so the molecule, although neutral, will be in an excited state. The molecule will, however, promptly return to the ground state and in so doing will radiate a characteristic series of spectral lines. Some of these lines will be in the ultra-violet region of the spectrum and consequently will have sufficient energy to liberate photoelectrons from the metal cylinder. With high tube voltages a single photoelectron will be sufficient to start a second avalanche and thus the entire process will be repeated over and over again.

It is possible, however, to construct counters in which the discharge can be stopped. These are known as self-quenching or fast counters. A self-quenching counter can be produced by adding to the usual filling gas a small amount of a polyatomic vapor, such as alcohol or xylene. These complex molecules strongly absorb ultra-violet light, and by this mechanism the photoelectric emission at the cathode is prevented. Most of the polyatomic molecules introduced to make self-quenching counters are vapors at room temperature, and these counters are apt to show a sensitivity which changes with temperature. A further disadvantage lies in the fact that some of the quenching gas is broken down (dissociated) at each discharge,

and so these counters have a limited life. A very satisfactory self-quenching counter can be made by filling the tube with 10 percent alcohol and 90 percent argon to a total pressure of 10 centimeters of mercury. With a non-self-quenching tube an auxiliary circuit must be used to stop the discharge.

Any counter will give counts when placed in a neutron field, but better results can be obtained with specially designed tubes. To detect slow neutrons the counter is filled with boron trifluoride, BF3, which is a gas at room temperature. A slow neutron may produce a nuclear reaction with the boron. This reaction liberates a considerable amount of energy, and the alpha particle and the recoiling lithium will have sufficient kinetic energy to produce heavy ionization which will trip the counter. By using the counter in the proportional range it is possible to obtain a count for each disintegration even in the presence of large beta and gamma intensities. The capture probability decreases with the neutron velocity so the reaction is not efficient for fast neutrons.

Fast neutrons may be detected through the recoil atoms which they produce when they collide with the gas atoms in the counter. The recoil atoms produce intense ionization, and hence if the counter is adjusted to the proportional range, the counter will discriminate against beta and gamma radiation. Fast neutron counters have a rather low efficiency because of the low cross section for the collision process. Neutron counting is complicated by the change in behavior with velocity, and the present neutron counters are far from satisfactory.

None of these devices gives an absolute measure of radiation intensities. It is therefore necessary to calibrate them in terms of known standards. This is not difficult if a gamma ray calibration is required in terms of roentgens. It has been established by careful measurements that 1 milligram of radium, in equilibrium with its products and enclosed in 0.5 millimeters of platinum or its equivalent, will produce an intensity of 8.4 roentgens per hour at a distance of 1 centimeter. The inverse square law can be used to calculate the intensities at other distances. Standard X-ray sources, properly aged and carefully calibrated, are available from the National Bureau of Standards. Calibration of X-ray measuring instruments should be carried out against primary standard ionization chambers or carefully calibrated secondary standards by a well-equipped laboratory such as National Bureau of Standards or by a reliable instrument manufacturer.

In making alpha and beta particle measurements quite different considerations enter. Radioactive materials emit particles in all directions with equal probability and in general a chamber or G-M tube

will intercept only a fraction of the total emission. For example, if the active material is spread in a thin layer on the bottom of the chamber, only one-half of the ejected particles will reach the gas and produce ionization. It is then necessary to calibrate the chamber in terms of a known radioactive material. Various members of the naturally radioactive series are useful for this purpose.

Photographic materials are also important tools for the measurement of radiation since high speed particles and high energy photons produce developable images. Although photographic films and papers lack the accuracy attainable in the laboratory by electrical methods, they still play an important role in radiation measurements. A film is one of the simplest detectors of radiation, is small and light, can be obtained with a wide range of sensitivity, provides a permanent record of exposure, and has no complicated electronic circuits to get out of adjustment. For many applications these facts more than outweigh the disadvantages of film processing, the time required to obtain a measurement, and the variations inherent in photographic materials.

TABLE I	Useful sensitivity
Emulsion:	range (roentgens)
Type K Type A Cine positive 5301 Cine positive fine grain 5302 Kodalith 6567 Kadabromide G-3 548-0, double coat 548-0, single coat	0. 05-2. 0 1. 0-10 5-80 40-400 70-700 400-8,000 2,000-10,000 5,000-20,000

Table I lists a series of emulsions that have proved useful for measuring beta and gamma radiation. It can be seen that a single emulsion will cover an exposure range of about 1-10.

Photographic film meters are usually made into packets of dental film size (1 1/4 x 1 3/4 inches) and covered with an opaque wrapping to protect the film from visible light. Any combination of suitable emulsions can be put into a single packet. A cross of thin sheet lead about 1 mm thick is customarily attached to the packet. This absorber is sufficient to stop all beta particles so any darkening under the cross will be due to gamma rays. The cross also serves to enhance the darkening due to gamma rays because of the larger number of electrons ejected from the lead. The regular wrapping is sufficiently thin to permit the penetration of all but low energy beta particles. Thus the film can be used to measure both beta and gamma exposures.

In general, film processing is carried out in accordance with the manufacturers' recommendations, but variations may be used satisfactorily. Whatever procedure is used, it is most important to control time and temperature as accurately as possible. The developer should be in a tank surrounded by a constant temperature bath, and the films agitated throughout development. The importance of time and temperature control, scrupulous darkroom technique, and the use of fresh chemicals cannot be overemphasized.

Special emulsions are now commercially available which are almost insensitive to visible light, beta and gamma radiations, but which will respond to heavy particles such as protons, deuterons, or alpha particles. These particles have such a low penetrating power that the emitting substance must be placed in direct contact with the emulsion. These emulsions are not used for personnel monitoring but rather to detect alpha particle contamination. These emulsions will detect alpha particles in the presence of strong beta and gamma radiation, and under conditions that make the operation of electrical alpha particle detectors uncertain if not impossible.

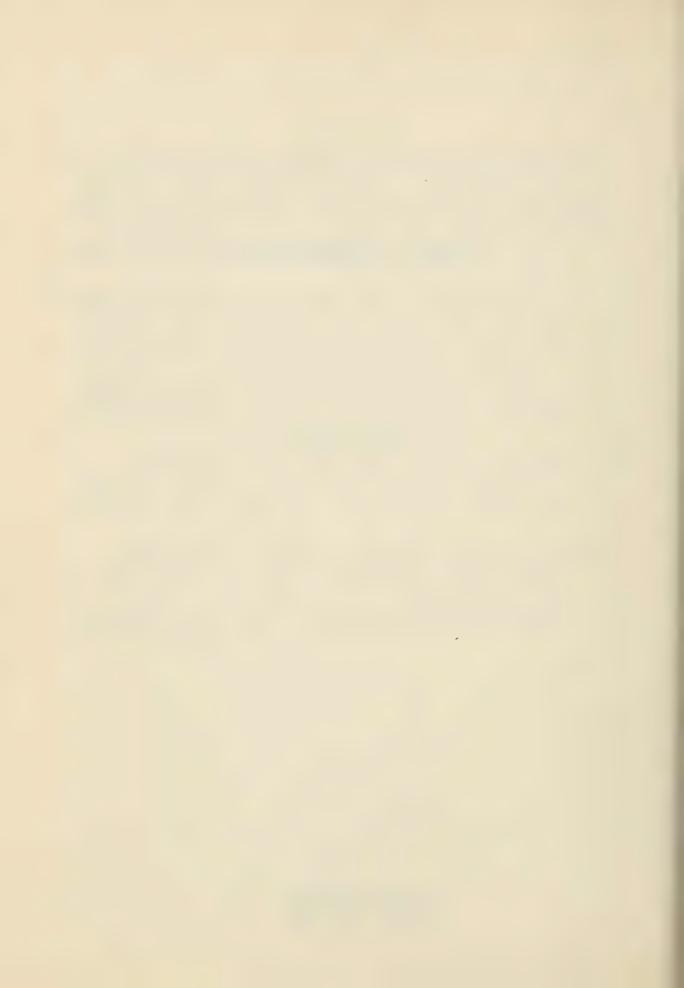
With weak exposures the plate will not be uniformly darkened and individual alpha particle tracks can be seen in a microscope. Since alpha particles are emitted with an energy characteristic of the emitting nucleus, the track lengths may frequently be used to identify the alpha emitter.

The various film emulsions can be used to make radio-autographs of specimens containing radioactive materials. By exposing sections of the specimen it is possible to determine the cross-sectional distribution as well. However, it must be emphasized that the resolving power of photographic emulsions for determining the precise position is limited, and it is scarcely possible to determine the location of radioactivity to less than 1/100 mm.

FUNDAMENTALS OF RADIATION PATHOLOGY

Elbert DeCoursey Colonel, M.C.

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The qualitative biologic effects of alpha, beta, gamma, x-ray or neutron radiation are apparently the same, the degree and localization of ionization being the basic factors. Energy is released in the cells by the formation of ion pairs. Grossly and microscopically only destructive effects are seen. I have not seen evidence of ionizing radiation effect that has been primarily stimulating.

According to Dr. Shields Warren, "alpha particles are about 100 times as effective in injuring cells as beta rays. Both are less penetrating and more destructive than gamma rays (hard x-rays of supervoltage)". This is in close agreement directly with their ionizing powers (10,000; 1,000; 1) and inversely with their ranges. Neutrons are apparently about eight times as potent biologically as physical equivalent amounts of roentgen rays.

Not the reading of an ionization chamber but the amount of radiation absorbed and the rate at which it is absorbed determine the effect on tissue. Thus well filtered radiation (say at 1000 KV of 500 r dose) will give a much greater dose in a field 10×10 cm. in tissue 10 cm. thick (with not even erythema of skin) than in a 3×5 cm. field. The same dosage over the entire body would be lethal.

Not all cells of an irradiated area are ionized. The discontinuous state of matter and of energy is an important consideration. Crowther has suggested that if a c.c. of air were irradiated at 1 r/sec. for 500 years, only one-third of the air would be ionized. This viewpoint is basic when considering ionizing effect on tissue either for intended therapy or from accidental or martial injury.

External or internal radiation differs in effect only as to location of the source and range, or penetrating power, of the type of energy (beta, gamma etc.) Total body irradiation from an external source will be the most important part of this discussion and its effects are quite different on the integrated organism from the effects of localized irradiation. When the source of internal radiation is in the blood stream, then the effect is that of total body irradiation. In internal radiation the physiologic action of the chemicals determines their localization in the body after absorption through the respiratory, gastrointestinal or integumentary systems. This, therefore, determines the location of the source of radiation from those chemicals that may be radioactive. That radioactive isotopes are handled no differently physiologically by normal cells than stable isotopes, is an accepted concept. For example, strontium acts like calcium and quickly localizes in bone. When absorbed from an aerosol, about 95% of the strontium disappears from the lungs in

an hour and 60% localizes in bone within four hours. Thus the radiation effect of aerosol Sr⁸⁹ (t/2, 55 days) after twelve hours is greater on the skeleton than on the respiratory tract. (Strontium, which is a strong, ordinary, chemical poison, has meanwhile occupied the blood stream.) On the other hand, 90% absorption of other bone localizers such as zirconium, yttrium and cerium aerosols is measured in days or weeks; therefore the lungs receive most of the radiation from such radioactive aerosols (MDDC-248).

Injury from radiation may not be immediately apparent. Some changes appear early and others may appear only after a latent period. Evidence of injury may not appear for months or even years. The progress of irradiation changes may be slow, continuous and of long duration. Within a half hour after onset of rather intense radiation, a decrease in mitotic activity may be apparent. Phagocytosis stops within a few hours. Mitosis is almost absent up to twelve hours, and occurs again after about 18 to 24 hours. Abnormal mitoses are most common during the second, third and fourth days. The blood lymphocyte count is perceptibly decreased in the first few hours following total body dosage. Oxygen consumption of tissues is decreased.

Edema, erythema (vascular dilation), increased mucus secretion, and perivascular round cell infiltration appears within a few days. Later changes are telangiectasis, fibrosis, atrophy, vascular occlusion and ulceration. Repeated irradiation necessitates long continued regeneration that may lead to neoplasia, such as skin carcinoma, fibrosarcoma, osteogenic sarcoma, lung carcinoma, and leukemia.

Fingerprint changes have been studied by Harvey and by Nickson. In 68% of radiologists, 55% of orthopedic surgeons using the fluoroscope and 40% of dentists who hold films, there was atrophy of finger ridges. The number of capillaries in nail fold areas seems to be correlated with hand radiation so that in young individuals capillaries seem to simulate those of old age. Flattening and atrophy of ridges, atrophic fissures perpendicular to ridges and epithelial proliferation are found on chronically exposed fingers. Acute radiation of 800 to 1100 r in monkeys resulted in temporary atrophy only.

According to the "poison" theory or "target" theory, changes in tissue components may be on the basis of the following factors: freeing of H and OH ions, the so-called activation of water; release of poisons from decomposed protein of cells; interference with enzyme systems, especially those with sulfhydryl (SH) groups; large molecule changes; and direct hits of ionizing particles on cell structures. Lesions also may be secondary to systemic changes such as radiation leukopenia. Cellular, intercellular and vascular changes are most important.

Cellular changes may consist of alteration of function, chromosomal alteration that effects subsequent progeny, or necrosis. Alteration in cell function may be seen in the loss of motility by granulocytes or the loss of motion of epithelial cilia.

The enzyme ribonuclease is inhibited by radiation. The basophilic stain in cell cytoplasm results from the ribose nucleoprotein present. Ribonuclease aids in the change from ribose nucleic acid to desoxyribose nucleic acid which forms the nuclear chromatin, and an excess of which must be present for mitosis to occur. This may be an explanation why one sees decreased numbers of mitotic figures, after irradiation. There are also mitotic figures showing fragmented chromosomes, lagging chromosomes, complete or partial adhesion of chromosomal pairs, asymmetry and/or tripolarity or Y-shaped figures. Mitotic injury has been divided into three stages: (1) "the immediate stage with inhibition of mitoses, pseudo-amitosis and pyknosis; (2) the intermediate stage, during which mitotic activity is practically absent; (3) and the later stage during which abnormal or multiple nuclei are formed as a result of a division of nuclei whose chromosomes have been injured." In a previous course Lt. Col. Carl Tessmer has listed the following microscopic changes that may be seen following radiation: (1) changes in staining characteristics, usually an increase in eosinophilic properties; (2) increased granularity, usually of cytoplasm; (3) vacuolation of a variable degree: (4) swelling of cellular components: (5) distortion of cellular structures; (6) cytolysis (loss of definitive borders); (7) pyknosis; (8) changes in Golgi's apparatus; (9) reduction in mitotic activity; (10) production of abnormal mitoses; (11) chromosomal changes (fragmentation, clumping); and (12) increased refractile neutral red staining bodies within leukocytes seen by vital staining methods.

Different types of cells differ remarkably in radiation response. Cells in mitosis are much more sensitive than resting cells. There is a common assumption that more primitive cells are more sensitive. Lymphocytes are more sensitive than the specialized neuron. That this is not a consistent rule is evidenced by the high resistance of the giant ameba and the high sensitivity of specialized ciliated epithelial cells of the bronchus (of mammals), and the greater sensitivity of mature over primordial ova and probably of spermatocytes over spermatogonea. Cells organized into a structural entity are more sensitive than when alone as in tissue culture. When the cytoplasm is involved, the effect is slight but when the nucleus is involved, the effect is apt to be lethal. A large cell with much cytoplasm will be more resistant than a small cell with a large proportion of nuclear material.

INTERCELLULAR changes vary from slight alteration to necrosis. Collagen fibers at first seem to be separated by edema, then became swollen and fuse into wide bands; later there is increased collagen which becomes homogeneous. The elastic fibers swell, fray and may be increased or decreased in amount.

VASCULAR changes range early from thrombosis to endothelial swelling and later from telangiectasia to partial or complete occlusion.

Changes in irradiated blood vessels play a most important part. Arteries

and veins show changes in all layers. The endothelium early swells and later proliferates sometimes to nearly fill the lumen; then there may be edema of the wall and decrease in the number of smooth muscle cells. The elastica is distorted or disappears. Sometimes the endothelium shows necrosis followed by thrombosis which in small vessels results in occlusion. The late changes of complete or partial occlusion from thrombosis or endothelial proliferation, and of telangiectasia in superficial vessels appear after several weeks. The collagen of the media shows its usual proliferation and hyalinization; this may require years. The lesions are slowly progressive. There seems to be increased cappillary permeability. Secondary nutritive changes in such a vascular bed may be profound.

All three factors, cellular necrosis, dense stroma and vascular deficiency result in the x-ray ulcerative lesion. This unfavorable environment along with the changed heredity of the newly formed cells discourage healing of the ulcer.

Not only are responses of tissues to various types of ionizing radiation qualitatively similar, but also are individual tissue effects to other stimuli similar. For instance, lipoid vehicles of injected drugs may produce abnormal mitoses; heat of cauterization may produce hyaline collagen; and many physical and chemical agents produce vascular damage. A combination of such changes, such as giant and irregular nuclei, hyaline collagen and thick hyaline blood vessels, however, are strongly presumptive evidence of radiation effect.

Relative radiosensitivities of various body tissues are fairly well established, but there are differences depending on whether the dosage is single, intermittent, localized, or total-body. We are mostly concerned with a single dose of total-body radiation. From the most sensitive tissue, lymphocytic (erythrocytic as judged by Bloom & Bloom), approximately decreasing sensitivity is shown by granulocytic tissue, then testis, gastrointestinal epithelium, skin, ovary, fibroblasts and their products, bone of adults, pancreas, liver, kidney, heart and striated muscle, and nerve tissue.

SKIN: Definite changes appear within 48 hours and more appear later. From sufficient dosage crythema is seen in two or three cycles, the first wave being between 1 and 4 days, the second wave between 8 and 28 days, and a third wave between 34 and 51 days. The early effects are directly from radiation, the later being largely secondary. Immediately epithelial mitoses decrease, the vessels dilate and inflammatory cells begin to infiltrate the cutis. During the second cycle there is desquamation of the stratum corneum, occasionally thickening of the granular layer, edema and vacuolation of the prickle and basal cells and of the upper cutis, all of which is usually followed by pigmentation. Collagen fibers swell, homogenize, and later proliferate to form a dense hyaline mass. Later the epidermal edema becomes intercellular, the basal layer degenerates and contains increased pigment, and near the edges of

the irradiated area chromatophores are darker. There is an inverse relationship between the amount of sulfhydryl (SH) present and melanin pigmentation. The infiltrate is increased through the cutis and around the hair follicles, sebaceous glands and sweat glands, which have shown changes in the order listed. Epilation appears about the third week. Follicles show cessation of mitoses, vacuolation of cytoplasm and sometimes necrosis. Chronic radio-dermatitis is characterized by hyperkeratosis, acanthosis, sparse or absent hair follicles and brittle and deformed nails in the hypertrophic type or in the atrophic type the skin is shiny, scaly, thin, and spider telangiectases are prominent. The epithelium and cells are thin, abnormal and disarranged, and the rate pags are flattened. Lack of secretions from the absent glands keeps the thin, scaly, irradiated epidermis dry and harsh. Trauma easily results in ulceration, and the ulcer then tends to persist for years. It is the regenerative edge of one of these ulcers that tends to become carcinomatous. The superficial vessels are telangiectatic and the deeper ones are in various states of degeneration. The corium is a dense hyaline mass of collagen. Areas of fibrin may appear in this otherwise old process as evidence of slow progression.

LUNGS: The initial changes are similar to those of skin. More cells appear in the alveolar walls giving a picture of pneumonitis, the alveolar lining proliferates and irregular cuboidal cells appear. Hyaline membranes may form in the alveoli. Elastic fibers become numerous. Large doses lead to progressive fibrosis.

GASTRO-INTESTINAL TRACT: The intestine has seemed about twice as sensitive as the stomach. The epithelium first shows edema, hyperemia, increased secretion, the reaction being established after about four days and reaching a peak, with ulceration, in one or two months. The epithelial cells may show early edema and decreased mitoses, then swollen nuclei with heavy stained chromatin and other atypical regenerating cells. Mucinous degeneration may be striking. The usual edems, hyalinosis, and giant fibroblasts, are seen in the connective tissue.

URINARY TRACT; In the kidney large doses may give extensive tubular degeneration and interstitial fibrosis, hyalinization and atrophy of glomeruli and thickening of Bowman's capsule. Later the organ appears small, has a thick capsule and shows dense hyaline interstitial tissue. The sensitivity is less than skin or liver but more than muscle or nerve. The ureter and bladder are relatively resistant but late ulcers may appear in the latter.

GONADS: In the ovary matured or maturing follicles are more sensitive than primary follicles. Treatment of ovaries in young adult by 500 r will temporarily sterilize. Edema, hemorrhages and later fibrosis occur. Corpora lutea are most resistant. The ovary, for destruction of function, has seemed to require about twice the dosage that is necessary to produce aspermatogenic testes.

In the testes, rats have shown necrosis of first order of spermatocytes on the third day, and vacuolations of the Sertoli cell cytoplasm during the latter half of the first week. The Leydig cells may show apparent increase with the tubular atrophy. There is variation in the sensitivity of different species.

ENDOCRINES: The adrenal cortex is fairly sensitive but recovers soon. The minimal changes are difficult to interpret microscopically. The weight increased surprisingly in rats after lethal radiation, adrenal cholesterol was decreased, and irradiated animals whose adrenals were protected had lower mortality than controls (Craver 1947).

The thyroid, pituitary, and pineal glands are fairly resistant.

EYE: Conjunctiva, cornea and iris are radiosensitive in that order. Radioconjunctivitis appears quicker than the dermatitis and during the third week usually becomes mucopurulent along with keratitis and bleaching or hyperemia of the iris. The epithelium reacts as does the skin. In the cornea the peripheral cells are swollen and irregular in shape and the substantia presents enlarged interspaces. Pigment clumps in the chromatophores of the iris; later this occurs in the choroid. The retina is considered more resistant than the lens. The lens is also resistant, the young being more susceptible to cataract which may show equatorial and posterior cortical cellular proliferation.

BONE: Eburnation and death without leucocytic reaction or sequestration er zone of demarcation are the effects of radiation to bone. Osteoblasts and osteocytes may disappear leaving the lacunae as empty spaces. The ivory-like texture is distinct as dense zones in the roentgenogram. Lack of osteoclasts, as the more radiosensitive bone cells, and therefore decreased bone absorption may be a factor. There is increased brittleness. Cells of the epiphyseal cartilage are sensitive and the normal columnar pattern is changed; 1200 r in children stops growth and prolonged fluoroscopy over the epiphysis in setting a fracture in a child must be avoided. Chondroblasts are also sensitive but hyaline cartilage is relatively insensitive. Perichondritis as in the ear, nose, and larynx develops late, sometimes after years.

The irradiated heart, which is resistant, may go into auricular flutter or fibrillation. Fatty degeneration, edema and cellular infiltration may be seen.

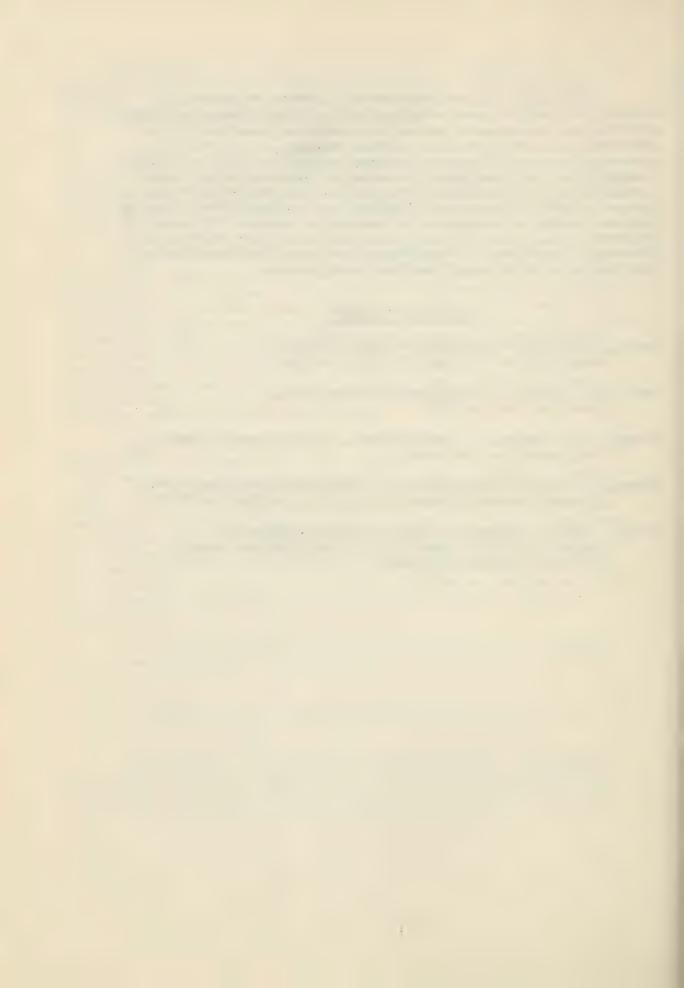
The nerves and ganglion cells are very resistant but in an irradiated area may show changes secondary to the vascular effect.

Body weight decreases after total body radiation. Most viscerol organs are affected less than body weight; muscle weight is parallel to body weight and spleen, thymus, gonads and gonadol fat are reduced out of proportion in rats (Brues et al. 1946). Except for radiosensitive organs, the weight loss is similar to that of inanition.

The lymphopoietic and hemotopoietic tissues are strikingly altered. Not only is grave atrophy visible, but also there are secondary effects of hemorrhagic tendency and increased susceptibility to infection, as in other profound aplastic anemias. A heparin-like substance is present along with prolonged clotting as well as prolonged bleeding time. No leukopenia is present in the normal animal cross circulated with the irradiated cat. Rabbits with regenerative anemias induced by phenyl hydrazine or bleeding when irradiated, 500 r, show no increased anemia or retardation in recovery as compared with controls, (Jacobson 1948). This would also seem to indicate that rubrablasts or other early progenitors of erythrocytes are not as radiosensitive as erythrocytic cells in non-stimulated, normal marrows.

COLLATERAL READING

- Warren, S.; Effects of Radiation on Normal Tissues, Arch. Path 1942, 34 and 1943, 35. (Reviews).
- Lea, D. E.: Actions of Radiations on Living Cells, MacMillan, New York 1947
- Liebow, A. A., Warren, S., and DeCoursey, E.: Pathology of Atomic Bomb Casualties (In Press)
- Bloom, W. (Editor): Histopathology of Irradiation From External and Internal Sources, McGraw-Hill Book Co., Inc. New York 1948
- Tullis, John L.: Response of Tissue Toward Body Radiation Project NM 007 039, Report No. 11, Naval Medical Research Institute, Bethesda, Maryland



PATHOLOGIC ANATOMY OF RADIATION EFFECTS OF ATOMIC EXPLOSION

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Before considering the radiation effects on the systems of the body, it is important to consider the relationship of lesions and time of death. In Japanese patients dying within two weeks after exposure there was histologic evidence of radiation in the lymphoid tissue, bone marrow, blood, gonads, gastrointestinal tract, and skin that was not manifested clinically. In the group dying in the third to sixth weeks, bone marrow changes predominated, while neutropenic ulcers and hemorrhages were very common. The general nutritional state declined. Gross changes were at the peak. Those dying in the third and fourth months showed beginnings of recovery in bone marrow and hair regeneration. Testicular changes remained prominent. There was in increase in the number of emaciated patients. The poor nutrition was not based entirely on shortage of food, intestinal lesions and other factors playing important parts.

SKIN. The quickly visible changes, other than ordinary trauma and burns, in Japanese affected by an atomic bomb were the pigmented areas that appeared in the first few weeks and persisted. These had such sharply demarcated outlines that they were considered as thermal flash burns. Development of what we have recognized as ionizing ray skin burns was not seen. There were a few early cases with bullous edema that may have been from gamma rays. Epilation appeared mainly on the scalp, ocasionally more on one side than the other, but far less commonly in the axilla, pubic region, and eyebrows.

Microscopically the hair follicles showed distinct changes both in the epidermal and dermal coats. Adequate early specimens were not obtained, but in the fourth week the internal root sheaths could not be identified, the external sheath (continuous with the malphigian layer of the epidermis) being continuous with the hair shaft. Vascularity of the papillae was reduced, and the adjacent epithelium was atrophic. Pigment was irregularly clumped. The dermal coat showed thickening both of the inner hyaline membrane and the cellular fibrous layer. In pushing the base of the hair toward the surface a continuous shrinking in the bottom of the follicle occurred until regeneration took place with new cells over the papillae in a manner similar to ordinary hair replacement. There was also atrophy of the sebaceous glands, but this was also present when old hairs were replaced in the normal individual.

Some of the sweat glands were small, their cells occasionally vacuolated and pyknotic, and the basal membranes thickened. Evidence of radiation on the skin was not definite. Third degree flash burns could also be expected to have some radiation effect, but interpretation was difficult. At the edge of the burn areas there was hyperpigmentation in basal cells and chromatophores. Depigmentation of flash-burned skin in individuals nearer the explosion and hyperpigmentation in those further away were unexplained features. Some thinning of epidermis, hyperkeratosis, ironing out of papillae, and hyperpigmentation of basal cells were found in the scalp. Vascular and collagen changes were minimal.

PITUITARY. Large basophilic cells with much cytoplasmic vacuolation appeared in 25 percent of the males dying in the third to sixth weeks. Because cells of this type are found in mammals after castration, they are known as "castration cells." In the second and third months large basophils were found, only a few being vacuolated.

ADRENALS. In the first two weeks there was a loss of lipoid in the cortex, but in the next months the cortex progressively lost its orange-yellow color and was distinctly thin. Microscopically, most cells were granular rather than foamy, and the atrophy was most marked in the outer zona glomerulosa, contrary to what was expected. When foam cells were present, they were usually in the inner layer. The medulla was normal, usually.

HEART. Epicardial petechiae were found within the first two weeks, and there was microscopic evidence of some perivascular and rare muscle edema in the myocardium. These changes continued to be present during the second month when myocardial hemorrhages were also seen. After the second month distinct irradiation changes were rare.

LUNGS. Only the slight perivascular edema of the pleura that appeared in the first two weeks might be a primary radiation effect.

Hemorrhagic and necrotizing pneumonia were common after the first weeks, as secondary lesions.

GENITOURINARY SYSTEM. Except for hemorrhagic manifestation, there were no primary lesions in the kidneys and ureters. In the hemorrhagic stage of the radiation disease, mucosal hemorrhages in the bladder night result in necrotizing ulceration without evidence of leukocytic infiltration. The prostate and seminal vesicles were not remarkable, except for an occasional neutropenic necrosis and the presence of a few spermatozoa that were morphologically normal in spite of the irradiation.

The testes showed intense changes in almost every cadaver. As early as the fourth day when the parenchyma had a normal appearance gressly, the histologic sections presented marked injury of the germinal epithelium, numerous cells of which were necrotic and free in the tubules and even in the rete testis. The number of mitoses was small. Sertoli

cells were increased in number. Mature spermatozoa were found even in later specimens with no spermatogenesis. Apparently uninjured spermatozoa appeared in the seminal vesicles. In the second month gross examination revealed little. A few necrotic germ cells remained, but most had disappeared, and phagocytic or infiltrating inflammatory cell activity was absent. A few bizarre cells still approximating the basal membrane appeared to be spermatogonia. Sertoli cells were more numerous. The tubules had started to shrink. At this time also the interstitial cells of Leydig were so prominent that some interpreters considered them hyperplastic. Some of the small interstitial vessels showed the most marked vascular change of any part of the body. Beneath the distinct thin endothelium was an eccentrically located mass of eosinophilic, homogeneous, refractile material that almost occluded the lumen. This change was often best seen near the tunica albuginea and was present also in the third and fourth months. It is not differentiated from sclerosis seen in older individuals. The interstitial tissue was less, but still prominent. The basement membranes were quite thick, wavy, and acellular. The tubules, more atrophic at this stage, were often hyalinized. Elsewhere Sertoli cells had replaced the germ cells, which were rare. In the third and fourth months the state of nourishment was poor, and specimens from the Dachau prison camp in Germany have been described as showing similar testicular changes.

Changes in the ovaries were much less striking. Gross changes, except as part of the hemorrhagic phenomena, were absent, even to the presence of a well-developed corpus luteum of pregnancy seen about the end of the first month after irradiation. Histologically, primary ova were usually present and only occasional specimens had a few atresic primary follicles. The absence of developing follicles was usual. There were no corpora lutea and the "resting phase" of the endomentrium reflected this. Amenorrhea was distinctly increased in Nagasaki, and a significant number of abnormal births and an increased death rate of the mothers in relation to distance from the explosion were found there.

GASTROINTESTINAL TRACT. This tract was one of the first to show gross lesions. Even before hemorrhagic manifestations the cecum or colon, particularly, might present a widespread change marked by swelling, green and yellow-gray coloration, and induration of the mucosa, sometimes with a pseudomembranous effect, and with much submucosal edema. Later mucosal hemorrhage might institute another cycle of similar change in the stomach or intestine. This change might begin with ulceration of the mucosa at the site of the hemorrhage and progress to a pseudomembrane or deep ulceragain, in the third and fourth months an enteritis, usually the distal portion of the large intestine but sometimes the small intestine and occasionally the stemach might present the most preminent lesion. In the small intestines only the tips of the folds might first be involved. These looked at first as though they had been dipped in boiling water and then became green or yellow-gray. A few specimens of small intestine

had a diffuse mucosal process. The large intestine in this late stage usually had a more widespread process that might extend from the ileocecal valve to the rectum. The thickened wall was characteristic. A pseudomembrane and ulceration were sometimes present so that the morphology was similar to that of bacillary dysentery. Much of the process here was not only an irradiation effect of the sensitive intestine, with lowered local ability to cope with intestinal microorganisms, but also probably more important, lowered antibiotic capabilities of the blood.

Microscopically the epithelium early contained extremely bizarre cells with giant hyperchromatic nuclei and multipolar mitoses. The swelling was seen to be from edema and some of the peculiar coloration from the absence of infiltrating leukocytes. Later, areas of mucosal ulceration with much fibrin, few leucocytes, and in the remarkably edematous submucosa quite a few histocytes, a few lymphocytes, and occasional eosinophils were seen. Plasma cells of the lamina propria remained numerous.

SPLEEN. The lymphoid elements here reacted to radiation as in the nodes. Early spleens were usually small, but occasionally showed the early swelling reaction. On section, they were dark red and not soft. The follicles were indistinctly seen, and the trabeculae were prominent. Besides the near absence of lymphocytes, large mononuclear cells were increased, and erythrophagocytosis and hemosiderin deposits were seen. In the second month the spleen was small and follicles were absent. There was a syncytial reticulum around the follicles in which the slight lymphocytic content of the organ was seen. Atypical large mononuclear pleohisticcytes, indistinguishable from Dorothy Reed cells, were found. Through the fourth month there was still some atrophy. Cccasional gérminal centers appeared, and the lymphocytic content showed evidence of recovery.

LYMPH NODES. The high sensitivity of lymphoid tissue to ionizing radiation resulted in tremendous atrophy seen as early as the third day. Lymphocytes almost disappeared, leaving a lacy framework that was histologically spectacular. A similar picture was found in the tonsils and other lymphoid tissue. Changes in the germinal centers might be necrobiosis, but a departure from normal was not marked except when the germinal centers disappeared, as they did in three-fourths of those who died in the first two weeks. The early gross appearance of human nodes was not known, but bombed animals showed some enlargement, softening, and a paler color. By the second week large atypical mononuclear cells. pleohisticcytes, considered by one observer as lymphoblasts, appeared. Again, these are the same as Reed-Sternberg cells but in a different environment than when they were first recognized and named. These cells These cells logically could be pathologic forms whose sensitive nuclear chromatin was deformed by the radiation. About the fifth week, the nodes were usually small and almost devoid of lymphocytes and germinal centers. Bizarre large cells were more numerous. Plasma cells, eosinophils, and mast cells, along with increased numbers of reticulum cells.

were present. Lymphocytes were more numerous in the fourth month but were still reduced.

BONE MARROW. The cellular picture of irradiated bone marrow was tremendously changed in the first week after the bomb explosion. There was almost total disappearance of blood-forming elements, excepting small islands of erythropoiesis. By the end of the week, reticulum began to proliferate and differentiated first into plasma cells and lymphocytes rather than granulocytic cells. This type of differentiation was predominant until the fourth week when myeloid differentiation was seen. Most marrows of those dying before six weeks were hypoplastic, but a few showed hyperplasia with lack of maturation. Most of the fatal cases of the third and fourth months showed hyperplasia, which in the femur was grossly evident as pink marrow extending through from one-third to one-half of the shaft. In these the maturation increased and more segmented cells were found in the peripheral blood and in infected tissues. A few of the older cases, however, showed aplasia with pink gelatinous femur marrow. Some grossly appearing hyperplastic marrows were really hypoplastic, some of the pink color coming from dilated blood vessels. Whatever the marrow picture, there was usually a profound leukopenia at some time in those dying in the first six weeks. Later leukopenia did not persist, and even some of those who died had leukocytosis. Anemia was greatest about the sixth week in those that lived, but in those that died anemia progressed even into the fourth month.

MISCELLANEOUS. Only secondary hemorrhagic or necrotic changes were found in the brain. No changes were found in the pancreas, except for some mitoses in the islet cells. The presence of any irradiation effects in the liver is a moot point.

SECONDARY EFFECTS OF RADIATION OF RETICULO-ENDOTHELIAL SYSTEM. Hemorrhagic lesions and leukopenic necrosis most prominently affected the irradiated body about the end of the first month. The pharynx and its connections, the gastrointestinal tract, the respiratory organs, and the skin manifested both changes. In addition, particularly the urinary tract, mesothelial linings, muscles, and all soft tissues, showed petechiae, purpuric patches, or large ecchymoses. These changes were outstanding clinically after the second week, but appeared in the viscera in the first week. The severity depended on the location of the larger hemorrhagic lesions. Hemorrhages in the linings of the pharyngeal regions, of the bowel, or of the urinary tract gave signs externally. Large submucosal hemorrhages as well as petechiae appeared in the kidney pelves and in the bladder and sometimes in the ureters. There were cases with prolonged clotting time as well as bleeding time, consonant with the presence of heparin-like substance as well as thrombocytopenia. Hemorrhages breaking through the epithelium of bacteria-laden surfaces often initiated the neutropenic ulcers, which in the pharynx were similar to acute agranulocytosis. Ulcers sometimes extended to the tongue, gums, buccal mucosa, lips, and even the skin to give the picture of

noma. Such ulcers also began without hemorrhage. Bacteria ordinarily nonpathogenic might cause serious consequences through the less of sufficient reticulo-endothelial reserves. Ulcers throughout the gastrointestinal tract were on a similar basis, as indeed, many of the diffuse mucosal changes might be. The necrotizing pneumonia appeared to be a part of this picture. There was little leukocytic reaction in these lesions, which overwhelm the patient and lead to death.

CASE HISTORY. A 29-year old man was at a distance of 0.7 km. from the explosion center. He was outdoors a few paces from a concrete building and was struck by a falling roof that inflicted slight head and neck injuries. There was nausea on 6 August 1945, and on the same day he vomited about 25 times. Malaise, accompanied by anorexia, began on 6 August and lasted until 10 August. He again experienced malaise from 21 August until he died on 1 September. Anorexia appeared four days after the second onset of malaise. There was epilation and gingivitis on 21 August, which persisted. The gingivae began to bleed on 30 August. On 25 August tonsillitis and purpura were noted. Both of these symptoms lasted until death. There was a high fever between 24 August and the time of death; and there was a productive cough beginning on 25 August with a hemoptysis on 30 August. The urine examined on 29 August was positive for albumin and negative for sugar.

Sections of marrow in this patient were hyperplastic, showing vascular adipose tissue crowded by a large number of young myelocytes. Mature polymorphonuclear leucocytes and even stab cells were rare. There was an occasional megakaryocyte. Occasional cells were found in mitosis. A few small cells with shrunken nuclei, thought to be normoblasts, also were found. Other important lesions at necropsy were: petechiae of the skin; epilation of the scalp; focal necrosis of the pharynx, tongue, tonsils, and larynx; necrotizing gingivitis; an abscess in the region of the right mandibular joint; necrotizing and hemorrhagic aplastic pneumonia; and minute hemorrhages of the gastrointestinal tract, trachea and renal pelvis.

REFERENCE

Liebow, A.A., Warren, Shields, and DeCoursey, E.: Pathology of Atomic Bomb Casualties (To be published)

RADIOLOGICAL DEFENSE

by

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RADIOLOGICAL DEFENSE

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General Considerations

For the purposes of military planning it must be assumed that atomic weapons may be employed against us in the event of our country ever becoming involved in another war.

In the defensive aspects of atomic warfare, because of the radiological hazards which may be created by atomic attack, the military commander and the medical officer will be confronted with many new and difficult problems in respect to conserving man power and sustaining morale.

To meet these problems a technology, new to military practice, has been developed and its application within the Armed Services is at the present time being extended both in plans and in training.

To this activity the term "radiological defense" is applied. More specifically it consists of those measures of a defensive nature intended to minimize the antipersonnel effects which may be occasioned by the injurious exposure of military personnel to the radiological hazards which may be created by atomic attack.

In atomic warfare, just as in any other form of warfare, risks must, and will, be taken. Such risks as relate to radiological hazards must be calculated and accepted in accordance with the demands of the military situation and in such manner as may be justified by the importance of the mission to be achieved or of the objective to be gained. A sound principle of economy of man power demands, however, that such risks as are avoidable, and at the same time unnecessary or unjustifiable, will not be taken. To accomplish this it is necessary that certain technical information relating to the existence, nature and seriousness of any such radiological hazard be obtained and that it be evaluated in accordance with appropriate standards.

The medical evaluation of such a situation requires that the medical officer be provided with such technical information as he may need to form the basis for his recommendations to the commander.

The commander in order to most advantageously make his decisions will require this technical information together with the recommendations of the medical officer in relation thereto.

The detection and measurement of radiation in field operations will usually be carried out by non-medical personnel or technical specialists of the line who are trained and equipped to do this type of technical work. As such they are technical representatives of the radiological defense organization rather than of the medical department.

The role of the medical officer will be that normal to his position. This will include specific responsibilities with respect to advising the commander in the medical aspects of radiological safety.

The technical aspects of radiological defense which are unique center around the techniques of detection and measurement of ionizing radiation and in the application of information so obtained in the evaluation of the military significance of such radiological hazards.

The operational aspects of radiological defense which are unique center around the detection and avoidance of radiological hazards in such manner as may be consistent with sound military practice. As such they consist of the employment by military personnel of the techniques of health physics and the principles of radiological safety adapted to the requirements of military practice and applied thereto in such a manner as may be feasible and practicable.

The implementation of radiological defense measures is in many respects similar to that required for chemical defense. While it is true that there is little similarity between the hazards which may be encountered, and while the techniques of detection are not similar, there is on the other hand a considerable similarity in the application of these quite different techniques both in the organization for, and in the conduct of, military operations.

While there is some degree of similarity with respect to the application of the principles of individual protection, there is a very much greater similarity with respect to the application of the broad principles of collective protection.

Because the problems of internal radiation (radioactive poisoning) are essentially toxicological in nature, there is a considerable similarity between the measures which may be taken to protect personnel against such hazards and the measures which may be taken to protect personnel against certain of the toxic agents of chemical warfare.

The pattern followed in the past in regard to planning, organizing and training for chemical defense is one which in general

outline may be followed in making similar preparation for radiological defense.

Each requires the employment of a sound philosophy which reflects not only appreciation of the military requirements but as well keen technical knowledge and practical, well balanced common sense.

Because the atomic weapon is characterized by such destructive and terrifying effects and because of the great emphasis which has been placed upon the unique characteristics of radiological hazards, we are today confronted with a serious psychological problem which involves military as well as civilian personnel and which demands at all levels of responsibility leadership which is intelligent, sound and effective. This situation requires a reasonably accurate evaluation of the probably effects of such weapons and the dissemination and interpretation of this information in such a manner as to gain the most widespread understanding and appreciation thereof. This represents one of the most important phases of radiological defense. Effective leadership and widespread appreciation of the facts are both essential. Failure is certain if either one or the other is lacking.

Even this, however, is not all that is required. It is necessary that there be developed a plan for radiological defense in order that the effects of atomic attack may be minimized as much as possible. It is further important that this be widely recognized and that there be general appreciation of the fact that such plans exist and that they are a direct answer to the question, "Well, what can we do?"

All military personnel will have some responsibilities of an individual nature with respect to radiological defense. Those in positions of command will have a particular responsibility with respect to the individuals and elements of their command. Still other individuals, or groups of individuals, will have specific duties of a technical or operational nature.

It is most desirable that all military personnel, regardless of position or rank, be suitably prepared by such indoctrination, training or experience as may be needed to enable them to fulfill to the best advantage such responsibilities as attach to the position, or duty, to which they are assigned. This responsibility will obtain regardless of whether it relates directly or indirectly to radiological defense, or whether in relation thereto it is specific or general in nature.

While interest in radiological defense may be great in the minds of many of us, we must not let it distort our sense of values.

There will continue to be other matters of fundamental importance and in relation to which radiological defense should be accorded only that consideration which is appropriate. On the other hand great harm may be done to the military effort of the future if radiological defense, and the broad implications thereof, are not given proper attention.

In this connection the very serious consequences which may arise from the "pyramiding of ignorance", must be stressed. This is an ever present problem and one which today we are not meeting very successfully. This must be recognized at all levels of responsibility and interests.

In matters of such a highly technical nature as may be involved in the technical and medical evaluation of a radiological hazard the careless or improper application of a little knowledge may become a very serious matter indeed.

In a similar manner the employment in radiological defense training programs of inadequately trained or poorly qualified personnel may lead to irrepairable damage. This poses a particularly difficult problem because of the need for rapid extension of training in radiological defense. This will continue until such time as there are developed within the military services sufficient numbers of personnel adequately qualified with respect to their ability to serve as reliable instructors and until there are sufficient numbers of personnel adequately qualified with respect to their assuming positions of responsible leadership in matters of radiological defense.

It is hoped that in time a suitable understanding of the problems of radiological defense may be universal among all personnel of the military services. That such a practical understanding may be developed is well within the realm of possible attainment. Admiral Parsons has suggested that such an understanding could be centered around a simplified "nuts and bolts" attitude. This is a goal for which those responsible for the development of radiological defense measures should strive. Man has learned to work reasonably safely with the serious hazards of high tension lines and of highly toxic and dangerous chemicals. It is not too much to think that man can learn to meet the problems associated with radiological hazards. The techniques to be employed are now reasonably well known. The measures to be applied in the way of planning, organizing and conducting such operations are known and have been successfully employed in atomic bomb tests. Training in both the technical and non-technical aspects of radiological defense is actively underway within the services at the present time. It is being progressively increased in scope and effectiveness as time and experience permit. The Armed

Forces Special Forces Project through its Joint Radiological Safety Training Committee has done a remarkably good job in providing guidance and in developing uniformity of content and training practice within the Armed Services. This will be more fully appreciated with time.

There is great danger inherent in attempts to over simplify the technical aspects of radiological safety. In this connection there are certain limitations which must be respected. This is particularly true in relation to the evaluation of the probable effects of ionizing radiation on living tissue and in an even more striking manner in relation to explaining and evaluating the hazards of internal radiation (radioactive poisoning). With this the medical officer will find himself deeply concerned.

Due to the nature of military organization effective radiological defense operations within the Armed Services can be achieved to a quite satisfactory extent if there is proper planning, organization and training, and if there is appropriate leadership at all levels of responsibility. To what extent this could be achieved by volunteer workers in a civil defense activity is a matter of considerable uncertainty. The need for radiological defense operations to be conducted in an orderly fashion by properly trained and qualified personnel in accordance with a sound plan of organization and operation, presents a particularly difficult problem with respect to the civil defense activities.

The Medical Specialist In Radiological Defense

Some medical officers will be given specialized training in the medical aspects of radiological defense in order that they may serve as special staff advisers, and in order that they may assist in the training of other medical officers in the more general medical aspects of radiological defense.

The mission of such a specialist will be:

1. At the direction of the commanding officer to establish, develop and execute plans for the medical aspects of radiological defense within the command.

The tasks and functions of such a specialist will include:

1. To serve as principal adviser to the commanding officer in all matters pertaining to the medical aspects of radiological defense.

- 2. To maintain sufficiently close contact with operations conducted within the command or subordinate units so as to be able to evaluate all radiological hazards which may be encountered.
- 3. To conduct the health protection program of radiological defense in such a manner as to support the overall Radiological Defense Plan of the command.
- 4. To conduct, or arrange for the conduct of such medical examinations or special medical studies as may be required and otherwise to observe the health status and psychologic effects in personnel engaged in all operations involving radiological hazards, and of all personnel prior to, and upon completion of, their assignment to such duty.
- 5. To provide for such health monitoring, including photographic dosimetry, as may be necessary to ascertain for medical purposes the degree of radiological exposure of personnel.
- 6. To provide, where necessary, such medical supervision as may be required in effecting the decontamination of personnel who have been in contact with radioactive material, and of their clothing and individual equipment.
- 7. To maintain a system of regular inspection of all radiological safety arrangements in order to assure complete compliance with the local radiological defense plan and with those established by higher authority.
- 8. To provide immediate care for personnel who may be injured while engaged in any activity involving exposure to radiological hazard.
- 9. To make adequate arrangements for personnel who may have received any radiological injury or who may be deemed to have received an injurious overexposure.
- 10. To supervise the professional and technical work of all medical and other personnel under his cognizance.
- 11. To report to the commanding officer as well as to higher authority within the Medical Department any serious infractions or radiological defense discipline and violation of radiological defense regulations.
- 12. To advise the Commanding Officer in the preparation of radiological defense regulations applicable to the command.

- 13. To maintain adequate records as required by local regulations and by higher authority and to submit all reports of radiological health operations required by the Medical Department and other higher authority.
- 14. To provide for such support from the Nedical Department as may be required by the radiological defense organization in the carrying out of the Radiological Defense Plan of the command.
- 15. To provide for such assistance as may be required in the general and specific training of personnel of the command in matters involving the medical aspects and the psychologic aspects of radiological defense.

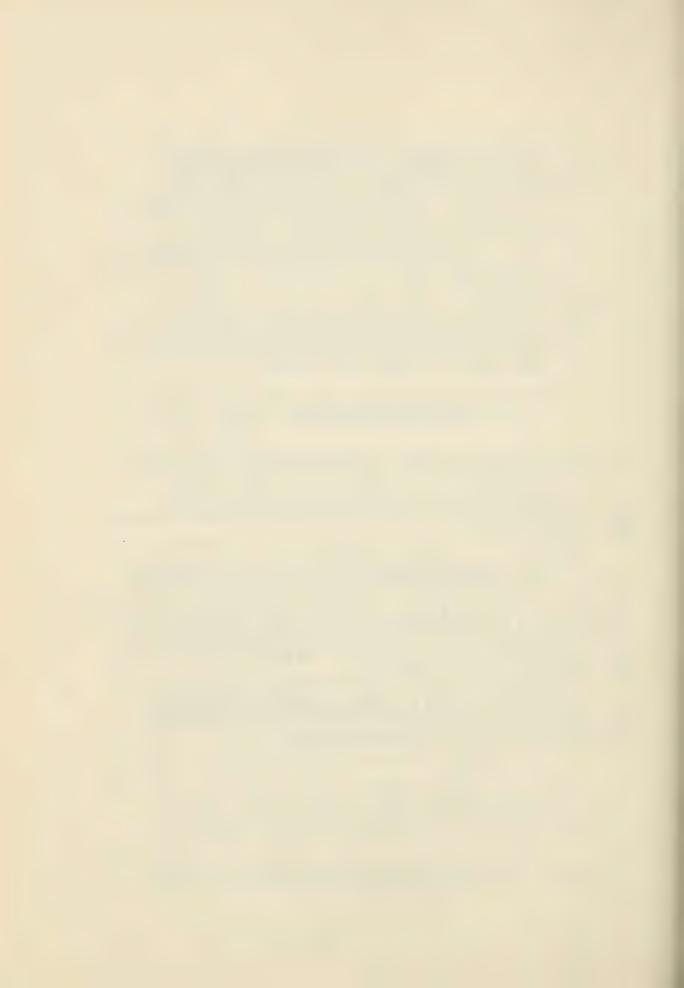
Radiological Defense Plan

The Radiological Defense Plan will be prepared as an Annex to the Operations Plan or as an Annex to the Station Pefense Plan.

It will be prepared for the Commanding Officer by the Radiological Defense Officer, with such assistance as he may require from the Medical Officer.

The body of the Annex will outline the general plan of radiological defense. Suitable appendices to the Annex will be written to cover the detailed aspects of training, administration, organization, operation, and logistic support. They will show how suitable integration or coordination is effected between the various operating elements and the radiological defense organization. One appendix will describe the integration or coordination of the medical activities with the radiological defense organization.

The personnel of the Radiological Defense Organization in the main will be officers and enlisted men of the line who have been specially trained in radiological defense.



THE DIAGNOSIS OF IONIZING RADIATION INJURY BY PHYSICAL
EXAMINATION AND CLINICAL LABORATORY PROCEDURES*

By

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Project NM 007 039

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^{*} Reference may be made to this report noting author, title, source, date, project and report numbers.

ABSTRACT

The symptomatology and diagnosis of acute and chronic radiation illness is discussed. Characteristic symptoms of the acute illness are nausea, vomiting, diarrhea, hemorrhagic manifestations, agranulocytosis followed by non-purulent necrotizing infections, and epilation. The blood picture is the most sensitive biologic index of exposure to ionizing radiation. Lymphocytopenia appears promptly after the single intense exposure. The symptomatology and blood picture of chronic exposure is protean. In order to evaluate the blood changes of chronic exposure, rigid control data must be established. The most significant blood change following chronic exposure is a depression of the mean leukocyte count of the exposed groups below the control groups. Dosimetry, the measurement of radiation intensities, must remain the basis of all protective measures.

INTRODUCTION

Prior to the advent of the cyclotron in 1931, sources of exposure to ionizing radiation were limited largely to x-rays, radium, and its disintegration products. The occupational injuries such as radiation burns, ulcers, and carcinoma (1), aplastic anemia (1,2), leukemia (3,4) and radium poisoning (5) were common among the pioneer workers. In recent years these occupational hazards have been reduced but not entirely eliminated by means of education, refinements in technique, and a better understanding of the biological effects of ionizing radiation.

With the installation of cyclotrons in many universities and scientific institutions and the development of the atomic energy industry, sources of exposure to ionizing radiation are increasing with great rapidity. In addition to the increased number of sources there are the artificial radioisotopes produced by the cyclotrons and the chain reacting piles that are being extensively distributed for scientific study and therapy of radiosensitive diseases. A hazard of contamination of domestic and wild animal and plant life by radioactive substances will occur if any notable volume of radioactive sewage from industrial and scientific services should develop. Again, if atomic warfare should occur, disposal of radioactive fission products will be impossible and widespread contamination of urban areas and watersheds may occur.

Injuries produced by the new sources and radioactive materials are no different than the injuries produced by the old sources. The problem today is qualitatively the same but quantitatively there are more people working with more potent materials. Prevention is the first consideration (6) and recognition of the injury is the second consideration in any program of preventive medicine. The purpose of this report is to outline the available knowledge on diagnosis of ionizing radiation injury by means of physical examination, and laboratory procedures. Dosimetry, the basis of prevention, will be referred to only for illustrative purposes.

In the course of this discussion frequent reference to animal experimentation will be made, where human data are lacking or inadequate. It must be fully appreciated as will be brought out in the course of this report, that the relationship between time of exposure and the appearance of signs and symptoms is not the same for man and smaller laboratory animals. All values for radiation dosage and laboratory procedures are the best possible estimate, based on available knowledge, and will have to be modified as more precise information becomes available.

Both acute and chronic effects may result from either internal or external ionizing radiation. The resulting clinical and laboratory picture is a function of the amount of radiation, its rate of delivery, and the depth dosage (7.8). This report will be divided into two parts dealing with the single intense exposure and the repeated exposure of lesser intensity.

Diagnosis of single intense exposure to ionizing radiation .-For the purpose of the present discussion a single intense exposure will be defined arbitrarily as a total body exposure of more than 25 roentgen units delivered within a few hours. An exposure of 25 r is set as the lower limit because the effects of lesser amounts are most difficult, if not impossible, to detect by clincial means (9). Whether lesser amounts may produce deleterious late effects is not known with certainty. The effect of exposure to ionizing radiation is determined to a considerable extent by the physical characteristics of the ionizing radiation concerned, that is, the type (alpha, beta, gamma, X-ray, or neutrons), the ability to penetrate (type and energy), and the rate at which the radiation is being delivered. With a single accidental exposure that may occur, these physical characteristics are usually known because of the nature of the experiment. Dosimetry (6,10) determines to a large extent the abovementioned physical characteristics. These physical characteristics are important because the clinical picture varies with the number of organ systems involved. Total body exposure to highly penetrating radiation in which all organ systems are affected, produces the severest picture but with a lesser amount of radiation than larger amounts absorbed superficially.

Symptomatology in man following the single intense exposure is quite well known from the experiences of the Japanese following the atomic bomb explosions over Hiroshima and Nagasaki (11,12).

A few hours after exposure to the atomic bomb ionizing radiations, nausea and vomiting appeared. This lasted for a few hours and then subsided for a variable latent period of days. The shorter the latent period the more severe the symptoms of recurrent nausea and vomiting, mucous or bloody diarrhea, purpura, epilation, and agranulocytic infections. In general, the tempo at which the disease progressed in the Japanese and the Bikini animals was a direct function of the amount of radiation received (11,12,13,14).

The latent period, the length of time between exposure and the development of symptoms, is of great interest. The duration of the latent period in mammals is inversely proportional to the amount of radiation received. With very large amounts of radiation, in excess of 10,000 r, the latent period becomes very short and death may occur within 24 hours or even while the radiation is being received (14, 15, 16-III). Each species has its characteristic latent period for

the development of the full symptomatology. In goats it appears to be 3-5 days; in swime it is approximately 5-7 days (14). In man it is probably longer. It is important to remember that with short latent periods death may occur before the full syndrome develops.

In the case of ionizing radiation that can penetrate only a few millimeters of tissue, signs and symptoms are limited to the surface of the body. Raper (17) has described the effects of beta radiation upon the skin of rats. Robbins, et al., (18) have described the effect of scattered cathode rays on the skin of man. In general one can state that the effects upon skin resemble thermal burns and that anything from erythema and massive vesiculation, to full thickness destruction of the skin may occur. Cutaneous changes are manifested by 1-3 stages depending upon the intensity of the radiation. For full details the reader is referred to the articles by Robbins (18), Raper (17), and Ellinger (19).

The early hematologic responses of man to single intense exposures to ionizing radiation is not well known. Unfortunately, the early blood changes were not observed in the Japanese hence reference will have to be made to laboratory animals in order to get an idea of what might be expected. There is no reason to expect any qualitative difference but there may be significant differences in sensitivity and rate changes in the peripheral blood.

The hematologic responses of laboratory animals to single intense exposures to penetrating ionizing radiation are quite uniform (9, 16, 20, 21, 22, 23). However, following exposure to less penetrating radiation the blood changes may be fleeting, slight or absent despite severe superficial injury.

Beginning shortly after exposure to penetrating radiation there is a prompt decrease in the total lymphocyte count which is most marked within 24-72 hours depending upon the amount of radiation received (9), (fig. 1 and table 1). Recovery following a non-lethal dose begins within a few hours or days. Developing simultaneously with the progressive lymphocytopenia is a moderate granulocytic leukocytosis which appears as two peaks approximately 12 and 24 hours after exposure in rabbits (9), (fig.1). If counts are not performed at about hourly intervals, one of the peaks may be missed. After the 24-hour peak there is a progressive decline in the granulocyte count for the next 4-6 days when there is a fleeting increase in granulocytes which is paralleled by a wave of bone marrow activity (24). This activity is short lived and the granulocytes again decrease. The subsequent course depends upon whether the exposure is lethal or non-lethal. In non-lethal exposures a sustained though small rise in the granulocytes appears around 15-17 days. In lethal exposures this sustained return of granulocytes is

absent (14). Granulocytic leukocytosis may not occur after very heavy radiation (16-II, 16-III).

Reduction in the number of platelets, red cells, and the morphologic changes in the leukocytes appear more slowly and are not so uniformly observed. In the Bikini goats and swine a marked shower of immature red cells appeared in the peripheral blood 10-12 days after the atomic bomb air burst (21). This phenomenon has been repeatedly observed in smaller laboratory animals (7). Atypical and immature leukocytes and nucleated red cells appear in the peripheral blood beginning 3-10 days after exposure (7.21).

In concluding the section of this report on the single intense exposure to ionizing radiation it is felt that the following can tentatively be stated regarding man, until actual observations substantiate or refute these suppositions. If no decrease in the total lymphocyte count occurs in the first 48 hours, usually the first 24 hours, the exposure has certainly been less than 25 r and symptoms probably will not appear. If exposure has been between 25-100 r a fleeting lymphocytopenia will develop and symptoms will probably be mild. If exposure is between 100-200 r the lymphocytopenia will be of greater severity and last longer. Severe symptoms of radiation illness and death will occasionally occur. If exposure is greater than 200 r the symptomatology of radiation illness will be much more severe and deaths will occur more frequently. The leukocytic changes particularly the early lymphocytopenia, will be marked.

The foregoing determination of a decrease in total lymphocytes or total leukocytes unfortunately cannot be predicated on a normal average for man or animals. The range of normal blood cell counts is great for all animals particularly in mongrel populations like man (23,25,26). Normal hematologic values of man will be considered in the second part of this report along with schemes for the detection of deviation from the normal ranges. Needless to say, in order to detect fleeting changes in members of the leukocyte population total white and differential blood cell counts must be performed every hour or so.

Diagnosis of acute radiation illness by the leukocyte count is obviously totally impractical under conditions of a catastrophe or atomic warfare. Hence the development of an easily-read casualty dosimeter is imperative.

The diagnosis of cumulative small exposures to ionizing radiation. The diagnosis of repeated small exposures to ionizing radiation presents an entirely different problem. The changes are insidious and progressive. If excessive cumulative exposure is not detected early, the changes may be irreversible and may lead to

serious and fatal diseases (1,2,3,4,5,7,22,27,28,29,30,31,32). At the present time 0.1 r/day has been set as the maximum amount of radiation that can be tolerated daily with impunity. Animal experimentation by Lorenz, et al., (33) on mice suggests that the tolerable dose of radiation for females should be set even lower because of increased incidence of ovarian tumors.

The physical characteristics of the radiation determine to a great extent the effects that will appear from chronic exposure. The penetrating radiation may result in generalized systemic and hematologic disorders in addition to the purely superficial effects of radiation with a very low degree of penetrability.

The physical characteristics of the radiation are usually known as a specific job hazard. Relative exposure to beta, soft x-ray, and gamma radiation is determined by suitable dosimeters (6,10).

The superficial lesions that appear are largely limited to the skin and eyes. Cutaneous lesions are apt to appear in fluoroscopists, radio-chemists, and radium handlers. An increased brittleness of the finger nails with a tendency to develop increased longitudinal ridges is common. Later there may be a loss of the integrity of the fingerprint due to patches of atrophy. Pigmentation, ulceration, and carcinoma may follow the atrophy. Epilation of hairy parts may occur. Impaired sensation of the finger tips commonly accompanies the above changes (1,34). In the eyes, radiation cataracts may occur at an early age (2). However, the alteration in the blood is the best biological index of chronic total body over-exposure to ionizing radiation.

Many investigators have called attention to the great variability of the blood of man chronically exposed to ionizing radiations. Leukocytosis, lymphocytosis, leukemoid reactions, leukocytic leukemias, erythrocytosis, reticulocytosis, leukemoid, thrombopenic purpura, aplastic anemia, and leukepenic leukemias have all been reported as produced by chronic exposure to radiation (1,2,3,4,5,7,22,28,29,30,31,32,35,36,37). The blood picture may be temporarily or permanently altered by many diseases and industrial intexications in addition to radiation. For example, infectious mononucleosis may affect the total and differential white blood count of young adults for many months after symptomatic recovery (38). Examples of industrial poisons which affect the blood are benzol (39,40) and heavy metals (1). Hence it is apparent that a "normal" range of blood counts for man must be established. This is difficult because the blood picture varies with age and to a variable degree with sex, pregnancy, meals, humidity, and temperature.

Osgood (26) gives the following "normal" values for individuals of different age and sex (table 2).

In naval personnel without any recent history or sign of disease (41) between the ages of 17-35 in the tropics and in a temperature zone, the total white count varied from 4,000-16,000. The total lymphocyte count was usually below 3,000 and rarely above 5,000. Probably 90 percent of the adult population will have total white counts between 5,000 and 11,000 per cmm. The 10 percent of adults whose counts are outside of this range may cause considerable consternation in a radiological safety program and lead to medicolegal problems.

Goldwater (39) has correctly called attention to the wide range of normal lymphocyte counts in his data and that of Osgood (26). The data on naval personnel confirm this concept. In addition Goldwater calls attention to the necessity of having comparable parallel control studies on subjects that are not subjected to any known toxic agents.

How are the blood changes of prolonged or repeated exposure to radiation determined? It is apparent that the average count is not dependable for the general population or specific age groups, hence base line complete blood counts must be performed on all individuals before exposure takes place. Subsequent counts should be performed at not less than monthly intervals. Notations on the occurrence of colds and infections, must parallel the blood records for without these base line records and a knowledge of each individual's response to infections an evaluation of leukocyte changes is more difficult.

A partial review of the literature (1,2,5,7,20,19,35,27,28,29,30,31,32,36,37,42) confirms the opinion that if any of the following alterations are noted in an individual whose usual blood values are known and who has been exposed to ionizing radiation it is presumptive evidence of excessive exposure until proved otherwise:

- a. A persistent depression of the total leukocyte count below 4,000 per cmm.
- b. A persistent elevation of the total leukocyte count above 15,000 per cmm. with an absolute lymphocytosis.
- c. A relative lymphocytosis with a low total count (4,000-6,000 per cmm.) that returns to base line range following removal from exposure.
- d. An increased mean corpuscular volume (MCV), a shift in the Price-Jones curve to the right, an increase in the mean corpuscular diameter (MCD).
- e. A reticulocyte count over 2 percent.
- f. An erythrocytosis:
 - (1) Red blood count over 5.8 million per cmm.
 - (2) Hamoglobin over 18.0 gm/100 cc. blood.

Many other phenomena have been suggested as hematologic evidences of excessive exposure. Changes in blood coagulation, prothrombin time, platelets (42), and morphologic changes in leukocytes (2) have been suggested. It is exceedingly difficult to evaluate the importance and the diagnostic value of these changes. A more recent observation on excessive exposure has been the description of refractile "Dickie bodies" in the lymphocytes (37). These refractile bodies are stained with neutral red in a supravital preparation and the authors believe that increased numbers of the bodies are specific evidence of exposure to radiation or industrial poisons. The procedure necessitates a flawless supravital technique which is not widely available, hence the technique may not be generally useful. Limited personal experience with swine and goats suggests that these bodies appear irregularly in lymphocytes as the lymphocytes age in the supravital preparations, hence a rigid time control might be necessary.

The foregoing criteria depend upon abnormalities in the enumeration or morphology of blood cells which arise from either depressed hematopoiesis, an increased lability of the hematopoietic organs, or abnormal maturation. The establishment of the presence of these criteria must of necessity be done without adequate controls that would not be permitted in the average biologic experiment. Hence it is much better to have some type of human control. This can be attained by establishing a comparable control group which are not subjected to any known toxic agent and performing parallel studies upon this group. Average values for exposed and control groups should be studied statistically to see if there are significant differences between the means of the two groups. In a comparable fashion the pre-exposure counts of the exposed group can be used as the control. If the average leukocyte count of the group for a given exposure period is significantly less than the group average leukocyte count of the pre-exposure period one can state with considerable certainty that excessive exposure to ionizing radiation or other toxic agent has occurred.

The following procedures will aid in determining the cause of any abnormal blood findings in a person suspected of having been excessively exposed:

- a. Remove the suspect from all possible exposure to ionizing radiation.
- b. Do differential counts of radiation on excreta, nasal swabs, and expired air in order to estimate the type and degree of internal exposure to radioactive isotopes.
- c. Study the blood at weekly intervals and compare with the pre-exposure base line leukocyte counts and search for an increase in the number of highly refractile, neutral red bodies in the lymphocytes.

d. Endeavor to eliminate other factors such as infectious lymphocytosis, infectious mononucleosis, virus diseases, benzol poisoning, and heavy metal poisoning.

SUMMARY AND CONCLUSIONS

- l. The diagnosis of a single excessive exposure to ionizing radiation by blood examination is not difficult. If serious exposure has occurred, a prompt, marked lymphocytopenia results and is followed by a characteristic sequence of events in the other members of the leukocyte population.
- 2. The diagnosis of repeated exposures to small amounts of ionizing radiation in an individual is much more difficult and uncertain. It requires in addition to blood studies, differential counts of radiation in urine, feces, and nasal secretions, and lastly the elimination of other industrial hazards.
- 3. The determination of repeated exposure to small amounts of ionizing radiation in groups of personnel by the statistical comparison with a control group or by statistical comparison of the pre- and post-exposure average leukocyte count is a reasonably accurate diagnostic procedure.
- 4. The main bulwark of protection from ionizing radiation must remain physical control of radiation intensities by established monitoring procedures and prevention of contamination of personnel by radioactive materials. This is essential because most of the signs and symptoms appear relatively late after the radiation injury has been sustained.

REFERENCES

1. Mieper, W. C., Occupational Tumors and Allied Diseases, Section on Roentgen Rays and Radioactive Substances, Springfield, Ill., Charles C. Thomas, 1942, p. 244-277.

 Selling, L., And Csgood, E. E., Action of benzol, roentgen rays, and radioactive substances, on the blood and blood-forming tissues, Downey, H., Handbook of Hematology, Vol. 4, 2963, Hoeber, P., New York, 1938.

3. March, H. C., Leukemia in radiologists, Radiology 43: 275-278,

Henshaw, P. S., Leukemia in mice following exposure to X-rays, Radiology 43: 279-285, 1944.

5. Martland, H. S., Conlon, P., and Knef, J. P., Some unrecognized dangers in the use and handling of radioactive substances, J.A.M.A. 85: 1770-1776, 1925.

Sullivan, W. K., Control of Radioactivity hazards, Chem. and Eng. News 25: 1862-1865, Jun 1947.

7. Warren, S., Effects of radiation on normal tissue. Dunlap, C.E., III, Effects of radiation on the blood and the hemopoietic tissues, including the spleen, the thymus, and the lymph nodes.

Arch. Path. 34: 562-608, 1942.

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8. Lawrence, J. S., Dowdy, A. H., and Valentine, W. N., The Effects of radiation on hemopolesis. MDDC-853. The University of Rochester, Rochester Project, Atomic Energy Commission, Contract W-7401-eng-19, 1947.

9. Jacobson, L. O., Marks, E. K., Simmons, E. L., Hagen, C. W., and Zirkle, R. E., Effects of X-rays on rabbits. Part II. The hematological effects of total body X-irradiation in the rabbit. MDDC 1174 Metallurgical Laboratory, University of Chicago. Atomic Energy Commission Contract No. W-7401-eng-37, 1947.

10. Safety Rules and Procedures Concerning Activity Hazards MDDC-992,

Manhattan District Declassified Document.

11. LeRoy, G. V., The medical sequelae of the atomic bomb explosion, J.A.M.A. 134: 1143-1148, 1947.

12. Warren, S., and Draeger, R. H., The pattern of injuries produced by atomic bomb at Hiroshima and Nagasaki, U. S. Nav. Med. Bull. 46: 1349-1353, 1946.

13. Tullis, J. L., and Warren, S., Gross autopsy observations in the animals exposed at Bikini, J.A.M.A. 134: 1155-1158, 1947.

14. Cronkite, E. P., and Tullis, J. L., In preparation.

15. Ellinger, F., Lethal dose studies with X-rays, Radiology 44: 125-142, 1945.

16. Henshaw, P. S., Experimental roentgen injury. I. Effects on the tissues and blood of C3H mice produced with single small whole-body exposure. II. Changes produced with intermediate range doses and a comparison of the relative susceptibility of different kinds of animals. III. Tissue and cellular changes brought about with single massive doses of radiation. IV. Effects of repeated small doses of X-rays on blood picture, tissue morphology, and life span in mice, J. National Cancer Institute 4: 477-522, 1944.

17. Raper, J. R., Effects of total surface beta irradiation, Radiology 49: 314-324, 1947.

18. Robbins, L. L., Aub. J. C., Cope, O., Cogan, D. G., Laugehr, J. L., Cloud, M. S., and Merrill, O. E., Superficial "burns" of skin and eyes from scattered cathode rays, Radiology 46: 1-23, 1946.

19. Ellinger, F., Biologic fundamentals of radiation therapy, Elsevier Publishing Company, Inc., New York, N. Y., 1941.

20. Minot, G. R., and Spurling, R. G., The effect on the blood of irradiation, especially short wave length roentgen ray therapy, Am. J. Med. Sci. 16: 215-240, 1924.

21. Cronkite, E. P., In preparation.

22. Furth, J., and Furth, O. B., Neoplastic diseases produced by general irradiation with X-rays, Am. J. Cancer 28: 54-65, 1936.

23. Charters, W. V., and Cronkite, E. P., In preparation.

24. Bloom, W., Histological changes following radiation exposures, Radiology 49: 344-348, 1947.

25. Farr, R. S., In preparation.

26. Osgood, E. E., and Ashworth, C. M., Atlas of Hematology, J. W. Stacy, Inc., San Francisco, California, 1937.

- 27. Henshaw, P. S., Further problems in X-ray protection. II. Irradiation injury and the tolerance dose, Radiology 44: 569-580, 1945.
- 28. Goodfellow, D. R., Radium and human leukocytes, Acta. Radiological 17: 1-50, 1936.
- 29. Goodfellow, D. R., Leukocytic variations in radium workers, Brit.
 J. Radiol. 8: 669, 1935.
- 30. Kaplan, J., and Rubenfeld, S., The blood picture in X-ray and radium workers, Radiology 26: 47, 1936.
- 31. Moldawsky, S. W., Uber den Einfluss der Berufsarbeit der Radiologen aud die erythropoetische Funktion des Knochenmarkes, Folia Haemat, 36: 145-173, 1928.
- 32. Paterson R., Effects of radiation on radium workers, Brit. J. Radiol. 16: 3-5, 1943.
- 33. Lorenz, E., Heston, W. E., Eschenbrenner, A. B., Biological studies in the tolerance range, Radiology 49: 274-285, 1947.
- 34. Warren, S., Effects of radiation on normal tissues. XIII.Effects on the skin, Arch. Path. 35: 121, 1943.
- 35. Warren, S., Blood findings in cyclotron workers, Radiology 39: 194-199, 1942.
- 36. Kornblum, K., Hoerner, F., and Henderson, S. G., The effects of radiation on the normal blood cells as determined by the blood count, Am. J. Roentgenol. 39: 225, 1935.
- count, Am. J. Roentgenol. 39: 225, 1935.

 37. Dickie, A., and Hempelmann, L. H., Morphologic changes in the lymphocytes of persons exposed to ionizing radiation, J. Lab. Clin. Med. 32: 1045-1059, 1947.
- 38. Cronkite, E. P., Unpublished observations on infectious mononucleosis.
- 39. Goldwater, L. J., Disturbances in the blood following exposure to benzol, J. Lab. Clin. Med. 26: 957-973, 1941.
- 40. Goldwater, L. J., Recovery following exposure to benzine (benzol).

 J. Ind. Hyg. & Toxicol. 23: 217-231, 1941.
- 41. Cronkite, E. P., Unpublished observations on blood counts of naval personnel.
- 142. Kaufmann, J., and Pierce, C. B., Coagulogram as critical indicator of irradiation effect; preliminary report based upon seven year survey of personnel of Department of Radiology, Royal Victoria Hospital, Am. J. Roentgenol. 55: 464-472, 1946.

Table 1. - Tabulation of the changes in white blood cells of rabbits after exposure to ionizing radiation*

	(10)	
ed before a to ts (days)	Heterophil	111140018
Time required before return to normal limits (days)	Lymphocytes	1 2000 200 10
Time of meximum depression in hours	Heteroph11	1 1 1 1 1 2 2 9 9 9 9 9 9 9 9 9 9 9 9 9
Time of maximum depression in hor	Lymphocytes	1 1 4 8 8 4 8 8 8 6 7
depression rcent	Herteroph11	0000 I# 05580
Degree of depression in percent	Lymphocytes	0088888800
Dose	(r)	\$ 2000 000 000 000 000 000 000 000 000 0

* From Jacobson, et al. (9)

Table 2.- Tabulation of the variations of the leukocyte count of man with age and sex*

	Number of Subjects	Age (In years)	Sex	Average in 1000's per cmm.	Range
Leukocyte	86 242 269	4-7 8-18 19-30	M&F	10,400 8,300 7,400	6,000-15,000 4,500-13,500 4,500-11,500
Neutro- philes, segment	241 120 236	4–14 15–19 20–30	M&F	% 38.0 48.0 54.0	% 18-58 25-75 33-78
Neutro- philes, band	219 378	4-13 14-30	M&F	3.0 0.8	0-10 0-5
Lympho- cytes	241 120 236	4-14 15-19 20-30	M&IP	48.0	21 -71 22 - 62 18 - 65

^{*} From Osgood (26)

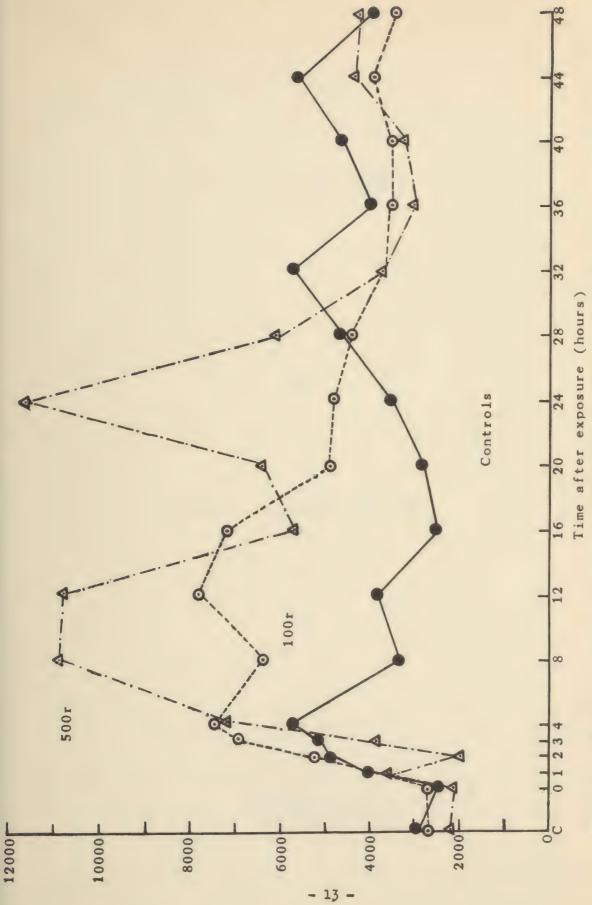


Figure 1 - The initial effect (during the first 48 hours) of total body X-irradiation on the number of heterophils in the peripheral blood, Jacobson, et al. (9)



THERAPY OF RADIATION ILLNESS

by

Captain R. H. Draeger, (MC), USN

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Introduction

The present status of the therapy of radiation illness is difficult to present largely due to the confused state of our knowledge on this subject. A large number of therapeutic agents have been proposed which have not been critically evaluated. Much research is being conducted in this field and new facts, almost daily, brought to light. Time will be required to assimilate this information and work out a rational therapeutic regime. It must be admitted that we now have little in the way of specific therapy. In view of these facts it is my intention to outline the medical problems with which we are confronted rather than to attempt to discuss a therapeutic regime in great detail.

The use of atomic energy is invariably associated with the liberation of ionizing radiation and the possibility of external or internal radiation injury. The atomic bomb is capable of exposing large numbers of individuals to ionizing radiation at the time of the explosion or later through contamination by fission products. The liberation of atomic energy in the uranium pile or in atomic power plants is also accompanied by a radiation hazard. Thus it will be seen that the problem of radiation injury or illness has become of great medical importance.

Radiation Illness

Let us now consider some of the problems of radiation illness.

Definition

Radiation illness is a symptom complex caused by the direct action of ionizing radiation upon certain tissues or organs and partly due to the systemic action of toxic substances released in the course of tissue disintegration.

Etiology

The etiology of radiation illness is ionizing radiation delivered as total body irradiation or the irradiation of certain radiosensitive portions of the body. The irradiation of the upper abdomen is most prone to produce radiation illness. Irradiation of the thorax is less

apt to produce radiation illness and the pelvis even less in comparable doses. Irradiation of the head, neck and extremities does not readily produce radiation illness.

The source of ionizing radiation may be external such as X-rays or the nuclear radiations from the atomic bomb or fission products including gamma rays, neutrons and beta particles. Internal radiation, produced by radioactive substances taken into the body, will also cause radiation illness. In all cases it is the ionization produced within the tissues of the body which is the cause of the radiation illness irrespective of the source or particular type of radiation.

The amount of ionization produced by an alpha, beta, or gamma ray will depend upon two factors; the total ionization and the specific ionization. Alpha, beta and gamma rays of equal energy will produce the same total ionization when completely absorbed. However, the number of ions per cm. of path will vary enormously. The energy of the gamma rays will be distributed over a path measured in meters while the beta rays will be stopped in a few cm. at the meat. Alpha particles, on the other hand, will only penetrate for a few microns.

From this it is evident that the effects of gamma rays will be highly diffuse regardless of whether the source is external or internal. The effect of beta rays will be somewhat more restricted while alpha particles will be confined to a few layers of cells immediately surrounding the source.

The amount of radiant energy absorbed by the body from a lethal dose of ionizing radiation is surprisingly small. I have made some calculations in this regard which are interesting if not instructive. Thus I requals 83.8 ergs per gram of tissue and when calculated for a 150 lb. man receiving 500 r, the total energy is 283 x 10⁷ ergs or 283 joules or 283 watt seconds which is sufficient to light a 50 watt lamp for 5.5 seconds or raise the total body temperature about 1/100 of a degree. The body absorbs about 40 times this much heat energy from a hot cup of coffee.

Although total body irradiation may produce ionization within every cell in the body, the initial harmful effects are manifest in the radiosensitive cells of a few tissues and organs located chiefly in the bone marrow, lymph glands, G.I. tract, skin and gonads.

According to the law of Bergonie and Tribondeau, the biological action of X-rays is greater the higher the reproductive activity of the cell. This law was formulated by work on the testes but its validity has been confirmed for many other tissues.

I will now ennumerate the most important tissues of the body in the order of their diminishing sensitivity to ionizing radiation:

- 1. Lymphoid cells.
- 2. Polymorphonuclear and eosinophilic leucocytes.
- 3. Epithelial cells including
 - a. Basal epithelium of the secretory glands.
 - b. Basal epithelium of the gonads.
 - c. Basal epithelium of the skin.
 - d. Epithelium of lung alveoli and bile ducts.
 - e. Tubular epithelium of kidneys.
- 4. Endothelium of blood vessels, plura and peritoneum.
- 5. Connective tissue cells.
- 6. Muscle cells.
- 7. Bone cells.
- 8. Nerve cells.

Diagnosis

Let us next consider some of the problems of radiation illness particularly as related to a disaster in which large numbers of individuals would be exposed to ionizing radiation. In such a situation it is extremely important to be able to quickly determine what dose of radiation each has received in order to segregate individuals into those who should carry on from those requiring hospitalization and therapy. Since the effects of irradiation are latent, it is likely that many individuals will be "psychological casualties" until the degree of their exposure is established.

Clinical or laboratory examinations do not appear to be adequate for this purpose since they require highly trained professional personnel and consume too much time. It might even be questioned whether the clinician will even be able to make a satisfactory prognosis prior to the onset of symptoms. A satisfactory dosimeter should be rugged, inexpensive and capable of being readily worn on the person. It should be capable of being read in a matter of seconds by relatively untrained personnel.

In order to illustrate this point I would like to show you several devices with which we have been working.

Two dosimeters were demonstrated. One consisting of a vicor glass rod contained in an aluminum case which had been worn by a goat at Bikini. This dosimeter had received about 10,000 r as indicated by a slight darkening of the vicor rod. Obviously this device does not possess sufficient sensitivity to be of value within the lethal dose range. An activated potassium bromide crystal was next shown which had been exposed to 100 r of X-rays (100 KV) and exhibited a fine blue color. It was explained, however, that this substance was not wave length independent and did not respond satisfactorily to hard gamma rays.

Symptomatology

Let us consider the symtom complex of radiation illness. It is convenient to divide the major symptoms into: general, gastro-intestinal, cardio-vascular, hematologic and neurological or psychic.

- 1. General Symptoms: Headaches, vertigo, debility, abnormal sensations of taste or smell.
- 2. Gastro-Intestinal Symptoms: Anorxia, nausea, vomiting, diarrhea.
- 3. Cardio-Vascular Symptoms: Tachycardia, arythmia, fall of blood pressure, shortness of breath.
- 4. Hematologic Symptoms: Leukopenia, thrombopenia, increased sedimentation rate.
- 5. Psychic Symtoms: Increased irritability, insomnia, fear.

Metabolic Changes

Alternations in body metabolism include the following:

- 1. Water Metabolism: Absorption of fluids from tissues into the blood.
- 2. Metabolism of Inorganic Substances:
 - a. Acid-base equilibrium; bi-phasic action with initial acidosis, lasting for 72 hours, followed by alkalosis.
 - b. Loss of minerals; concerning chlorides, sodium calcium sulfur and phosphates.
 - c. Relative increase of blood potassium.
- 3. Protein Metabolism:

- a. Increased total protein content of the blood.
- b. Increase of non-protein nitrogen content in blood and tissues.
- c. Increased nitrogen excretion with the urine.
- 4. Purine Metabolism:

Increased urinary excretion of purines.

5. Fat Metabolism:

Fall (sometimes increase) in serum cholesterol levels.

6. Carbohydrate Metabolism:

Bi-phasic action; initial fall of blood sugar (12-24 hrs) followed by a rise.

7. Gas Exchange:

Slight increase in oxygation, rise in respiratory quotient.

The mechanism responsible for the lethal effects of irradiation is not well understood; however, it may be worth while to examine some of the most conclusive evidence. In the light of recent investigations it appears that the toxic agents liberated during tissue break-down, following irradiation, may best be described as histamine-like in nature if not histamine itself for the following reasons:

- 1. Histamine is capable of producing most of the symptoms and metabolic changes of radiation illness.
- 2. Histamine is also capable of producing fatty changes in the liver similar of the changes seen following irradiation.

Daugherty and White have observed that leukopenia following X-ray irradiation is at least, in part, caused by the indirect action of tissue decomposition products. These authors demonstrated that the normal leukopenia response in mice was not present in adrenalectomised animals. However, a larger dose caused leukopenia apparently due to direct action upon lymphatic tissues. Torgersen, in Oslo, has demonstrated the role of tissue decomposition products in the production of radiation effects in the adrenal cortex by the irradiation of ears of rabbits.

In summing up this accumulated clinical and experimental evidence, the mechanism of radiation illness may possibly be explained as follows:

130

Irradiation of sufficiently large volume of the body results in the release of histamine-like substances or histamine itself. These substances induce the anterior-pituitary to secret corticotropic hormone, which in turn stimulates adrenal cortical activity. This stimulation results in exhaustion of the gland thus producing the symptoms of radiation illness. This suggests certain lines of therapy to be discussed later.

Therapeutic Measures

Any consideration of the therapy of radiation illness must take into account the fact that many cases of irradiation will be complicated by flashburn and blast injuries. Since the effects of the atomic bomb include blast, thermal and ionizing radiation, it is difficult to evaluate the relative importance of each of these factors individually; all three contributing to the death of many individuals. We are confronted with the possibility that the presently accepted treatment of burns, for example, may not be the best in concurrently irradiated individuals.

A large number of substances have been suggested for the treatment of radiation illness but so far few have proved to be of value. Folic acid and pyridoxine are of no value in mice if given after irradiation. Rutin also appears to be of no value.

The use of antibiotics to combat the tendency to infection and septicemia in the agranulocytic stage of radiation illness will no doubt play an important part in the future treatment of this condition.

Following the identification of an anticoagulant with heparinlike properties in acute radiation illness by Allen, it was hoped that the use of anti-heparin agents such as toluidine blue and protamine would favorably affect mortality but this has not yet been demonstrated.

Since blood production practically ceases for a period of days following irradiation, blood transfusions are probably of value in maintaining resistance to infection and the exygen-carrying capacity of the blood.

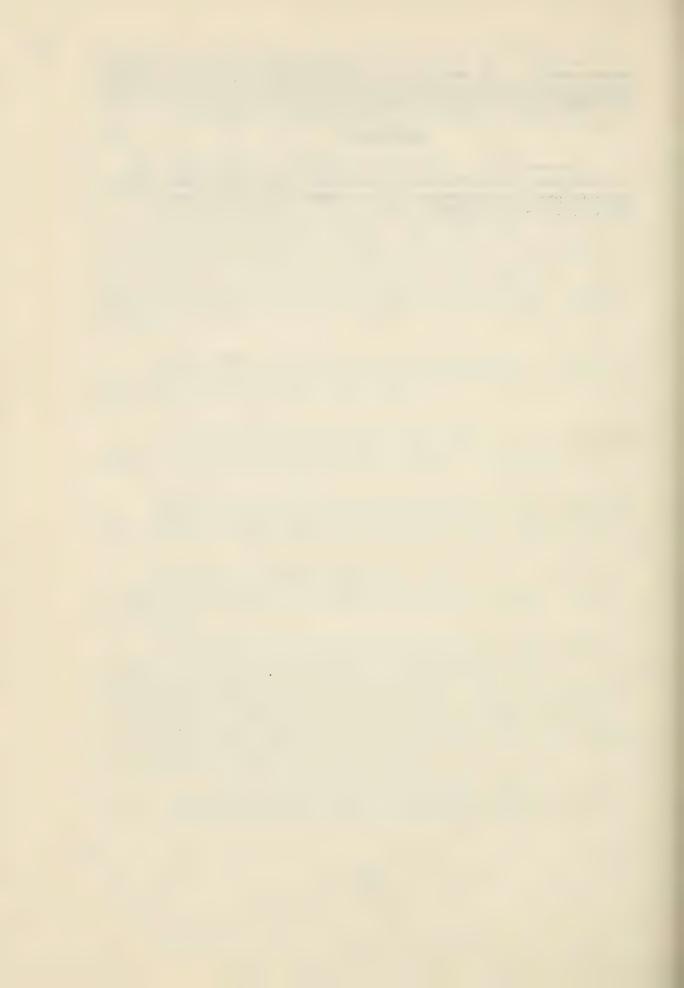
In 1946, Ellinger, reported that desoxycorticostrone acetate protects the liver against radiation fatty degeneration and at the same time reduces the X-ray mortality rate in mice. From this and other experimental evidence it was concluded that desoxycorticostrone would be useful in the therapy of radiation illness. Clinical studies in patients undergoing therapy have verified this opinion. This treatment appears to counteract the mechanisms largely responsible for the chain of events causing radiation illness.

Another point which cannot be too strongly emphasized is the need for immediate hospitalization of irradiated individuals with

proper sedation. It can be shown that irradiated animals are readily susceptible to injury from stress conditions such as chilling, fatigue and hunger which ordinarily produce little ill effect.

Conclusion

In conclusion I would like to point out the fact that much research work on the problem of radiation illness is now under way and important discoveries may be anticipated which will lead to better and more specific therapy.



PROTECTION AGAINST ATOMIC BOMBS

by

Maj. William W. Stone, Cml. C.

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PROTECTION AGAINST ATOMIC BOMBS

William W. Stone Maj. Cml C.

In considering protection against atomic bombs, the words "protection" and "defense" are almost synonymous. We will treat this subject by dividing it into two broad categories: passive defense and active defense. Because of the nature of this conference, emphasis will be placed upon those factors bearing a relatively close relationship to medicine. For completeness, howover, other aspects will be mentioned.

It is important to realize from the very beginning that the important effects of the atomic bomb against which protection must be developed are:

- 1. Blast or Shock Wave
- 2. Visible and Near-visible Radiation
- Nuclear Radiation
 Psychological Effects

I. Passive Defense and Protection

- 1. In considering all of the effects of the atomic bomb, it should be noted that these influences all decrease in intensity extremely rapidly as one moves away from the point of detonation. thus it is apparent that distance is always the best protection. In devising methods of protection, one always has the very difficult job of fighting against the extremely rapid increase toward the bomb of the forces capable of creating damage.
 - a. Primary shock or blast damage, is defined as the compressive and tearing action of the shock wave on the human body. When one interposes between the blast and the body an object of strength similar to that of an ordinary wall, this form of damage is effectively reduced. Primary shock is thus of importance only when a person is in the open and exposed simultaneously to lethal amounts of other effects of the atomic bomb. Living things are remarkably resistant to this form of damage and are much stronger in this respect than normal buildings. Underground shelters and normal reinforced concrete buildings protect against this effect up to very close to the point of detonation. This damage in its mildest forms is seen as petechial hemorrhages of the lung. In its severest forms major abdominal hemorrhages appear.

- b. Secondary shock or blast damage is extremely important and is defined as being due to flying objects hitting and lacerating the body. A shock wave is very much like an extremely strong wind which lasts for about a second. This wind is strong enough to throw the body many feet. It also breaks windows, knocks down plaster, and throws other objects around with great violence. When these objects strike a human or the human strikes an object, secondary shock damage, or trauma, results. There are many things that the individual can do for himself to reduce his chances of this type of injury if he has some advance warning of the detonation. It is obvious that he should keep away from the windows and that he should get flat on the floor or ground. One should avoid standing under overhanging cornices, beneath chimneys and other heavy objects which are easily knocked down. Underground installations or shelters greatly reduce this effect because very little of the air shock is transmitted through the ground and thence into shelters or basements. In Japan, this form of injury combined with burns accounted for most of the casualties. The rapid follow-up of the fire on the blast damage caused many fatalities among the injured. Injuries of this type require evacuation, treatment and hospitalization. In the case of primary shock damage there is an amazingly small boundary zone. One is either dead immediately or all right as far as this effect is concerned after a few minutes. There is much that can be done in the design of vital installations to reduce damage from these secondary shock effects.
- c. Flash burns are those injuries which are created by direct exposure to the visible and near-visible radiation emanating from the point of detonation. The thinest type of non-transparent material will shield effectively from this effect. Light colored clothing is particularly good as it reflects almost all this radiation. Dark colored clothing will not transmit this radiation but will catch fire and produce flame burns on the skin beneath the clothing. This form of damage is important only when the person is in the open and in direct line of sight from the point of detonation. Because of the nature of the atomic bomb, this form of damage occurs at greater distances than those caused by any other effect.
- d. Flame burns are those injuries which are produced by fires started in inflammable material or buildings. Those effects were very prevalent in Japan but would be expected to occur to a lesser degree in an American city. The possibility of fire and subsequent injury can be greatly reduced

by making structures less inflammable. Also, the development of adequate and large amounts of fire fighting equipment and trained personnel can furnish great protection. To reduce this form of damage it will be necessary to have fire fighting equipment and personnel so located that a major proportion will not be wiped out by the detonation. Reading of the accounts of Hiroshima and Nagasaki points out the complete inadequacy of Japanese fire fighting equipment and procedures. In both cities, about 90% of the equipment and personnel for these duties were wiped out immediately. Major efforts should be placed on reducing the possibility of this type of personnel damage, not only because of its capabilities of producing a very large number of casualties, but also because these casualties subsequently need even larger amounts of personnel and equipment for treatment and hospitalization.

- e. Nuclear Radiation. The utilization of nuclear radiation in warfare presents completely new problems for both the military and the civilian. These effects are not only important but complex. They constitute the primary reason for this conference. In considering this subject we will break it down into several categories. The most important division is into external and internal hazards. Another division which is of importance and helps to clarify the situation is to divide these effects into immediate and delayed hazards. For all nuclear radiation effects the general statement is again pertinent that distance is by far the best protection.
 - (1) Prompt or immediate radiation. By prompt radiation we mean those forms of damage which are produced in a matter of a few thousandths of a second after detonation. With the atomic bomb roughly 99% of the nuclear radiation produced comes out in the first small fraction of a second after the detonation. These radiations emanate from the detonating bomb and the ball of fire is formed immediately afterwards. They consist of penetrating radiations which come from outside the body. Hence, all prompt nuclear radiation is described as an external hazard.

Large amounts of gamma rays come out almost immediately from the detonation, radiating in all directions. These rays travel in a straight line as does light. They are highly penetrating and it takes a large amount of material to absorb and stop them. It is of importance to realize the directional and shadow producing characteristics of this radiation. One does not need shielding on all sides but merely between one and the point of

detonation. In shielding against gamma radiation, the important thing is the weight of the material which is between you and the source. The chemical characteristics of the constituents are of no importance. Lead is often used in laboratories where gamma radiation or x-radiation occurs. This is a suitable substance because it occupies a very small volume in comparison to its weight. Equal weights of water, steel, concrete or wood are just as effective except for their space consuming characteristics. The effectiveness of a shield is most often described by means of thickness of the material which is necessary to reduce the intensity to one-half (1/2) the initial amount. This is called the half-thickness of that material. It is useful to know very rough half-thicknesses for common construction material. They are:

1 . -

1 for steel
3" for concrete
4" for wood or earth

Noutrons also constitute an external hazard at the time of the detonation. They are not as effective at great distances as the gamma rays but require consideration. Because neutrons are uncharged particles, they are difficult to stop and shield against. Shielding is not as simple as in the case of gamma radiation because weight of the shielding is not the important factor. Instead, the important characteristic is the ability of the particular chemical or element to slow down and then capture neutrons. The neutrons which occur in the detonation of an atomic bomb are essentially fast neutrons. Substances such as cadmium and boron capture slow neutrons to an amazing degree. Because these neutrons are not slow these substances are of no particular value in defense against the atomic bomb. The best substances are those with low atomic weights. Hydrogen, the lightest of all substances, is the best; hence, in shielding against neutrons the best substances for their weight are those containing large amounts of hydrogen. Such shields would be materials like water or paraffin. Very rough half-thicknesses can be given for common structural materials and are as follows:

Somewhere between 3" and 12" for steel About 6" for concrete, earth or wood About 6" for water.

Neutrons like gamma rays also travel in a straight line from the point of detonation, going in all directions. Hence the shielding need be only between the person and the source.

(2) Delayed radiation. This is the one percent of the nuclear radiation which does not come off immediately but which comes from the decay of the fission products produced by the nuclear explosion. In an air burst, where the fire ball and mushroom cloud containing the fission products, go up in the air to be dispersed by the wind, this delayed radiation is negligible. In an underwater burst, or possibly a surface land burst, a base surge like Test BAKER at Bikini will probably occur. This cloud moving along close to the ground contains a large proportion of the fission products. As this cloud sweeps out over ships or cities it surrounds buildings. people and equipment. The radiating material is then extremely close to a person. And the relatively small amount of radiation that is left after the detonation is greatly enhanced because of its proximity. This base surge, in comparison to the mushroom cloud after the air burst produces radiation intensities on the ground which are higher by a factor of thousands, perhaps millions. This is due solely to the fact that the base surge can surround individuals on the ground. When it is realized that at Test BAKER this base surge moved over an area of roughly five square miles, this is seen to be a very real hazard. It, of course, takes time for this cloud to move, and, as the radiation from it is only of importance when it surrounds the point in consideration, there is available a varying amount of time in which to get out of the way or to dodge the cloud. This base surge moves with varying speeds. Initially it spreads out at about 50 mph. Its speed constantly decreases until it reaches zero at its outer limits. For this cloud to spread over its maximum area requires several minutes. If one is in a city, great protection will be afforded if one gets down into a basement or sub-basement, or into an airraid shelter. It is of importance also to note that this radiation from the base surge is non-directional as it comes from all points in the cloud. Hence any shield which is devised must be on all sides, including on top of, the location considered.

Delayed gamma radiation from the base surge is similar to prompt gamma radiation except in its non-directional characteristics. The shielding requirements are similar to the previous situation in that the same half-thicknesses are applicable.

There are no delayed neutrons of significance; hence, special shielding is of no importance for this problem.

In the delayed situation we also have important beta radiation. Prompt beta radiation does occur but does not travel a very great distance from the source because of the efficient shielding furnished by air. Where the base surge is surrounding the location in question, beta radiation is important because the half-thickness of air is roughly 3 or 4 yards. Normal clothing furnishes sufficient shielding to beta radiation. Similarly thin walls and the glass in windows are adequate. It is of course non-directional and comes from all sides. The extent of the external hazard furnished by beta radiation is not well understood. It is believed comparable to that of gamma radiation when a base surge has been created.

Alpha radiation, of course, occurs from the non-fissioned material; in other words, plutonium or uranium is its source. This radiation constitutes no external hazard as the skin furnishes adequate shielding. All the alpha rays are absorbed in the epidermis with no resulting damage to living tissues.

(3) Nuclear radiation (internal). With an internal hazard we have the situation where radioactive materials, either fission products or non-fissioned material, gets into the body through inhalation, ingestion or injection. This is, of course, a delayed hazard and is possible only where one is in the base surge, in the mushroom cloud, or working in an area over which the base surge has previously passed. The internal hazard occurs generally only where there is also an external hazard. If one is exposed to the base surge or is in the mushroom cloud, the external hazard is often lethal in its own right without any consideration of an internal hazard. Particularly if one is working in a highly contaminated area after the detonation, there is a significant but not necessarily lethal amount of external hazard, but there is also a very great internal hazard. This is created by disturbing the deposited material by kicking up dust and is usually gotten into the body through inhalation. An additional hazard exists from eating with contaminated hands and thus getting the active material into the body through the mouth.

It is important to realize that in the case of an atomic explosion the very small weight of active material is dispersed in the form of a true gas or vapor. Almost all of the active material adsorbs onto particles of dust or droplets of water. *Protection against these particulates is*

probably achieved with the use of ordinary gas masks containing modern filters. These contaminated particles have a size range of from 0.1 microns to 10 microns. The filters on modern gas masks such as the assault mask are believed to be quite adequate. These filters are extremely efficient. It is quite possible that new masks will be coming out which have adequate protection for atomic warfare, biological warfare and chemical warfare. Such a development of course is highly desirable.

It is probable that protective clothing will be required for workers entering contaminated areas. It would probably be permeable clothing. Its main requirement is that it should be disposable. Its functions would be to keep contaminated material from the skin and possible later entry into the body. Disposability is desirable as these materials cannot be rendered harmless by any physical or chemical means.

Collective protectors with filters or inclosed air conditioning systems are probably indicated for vital installations and underground shelters in anticipation of atomic warfare. Such items would prevent the entry of the highly contaminated air of the base surge into installations which otherwise would furnish adequate protection against the effects of the atomic bomb.

The development of decontamination techniques and facilities is indicated to reduce the very long term possibility of personnel becoming contaminated and later having active material enter the body through the oral and digestive tracts. Such techniques will probably consist of washing away, carrying away, or burying the active material.

f. Education. In an attack on a modern city it is believed that approximately 50,000 mortalities would be created by a single bomb. It is felt that if the individual civilian and soldier in these cities or installations were adequately trained as to what he could do for himself after the detonation occurs, that perhaps 10,000 lives could be saved. Exactly how much and what kind of education this requires is not yet known. It is believed to be relatively simple and is obviously important. The development of atomic defense for the individual will be the subject of much work in the future. Also of importance is the education of large numbers of personnel, both civilian

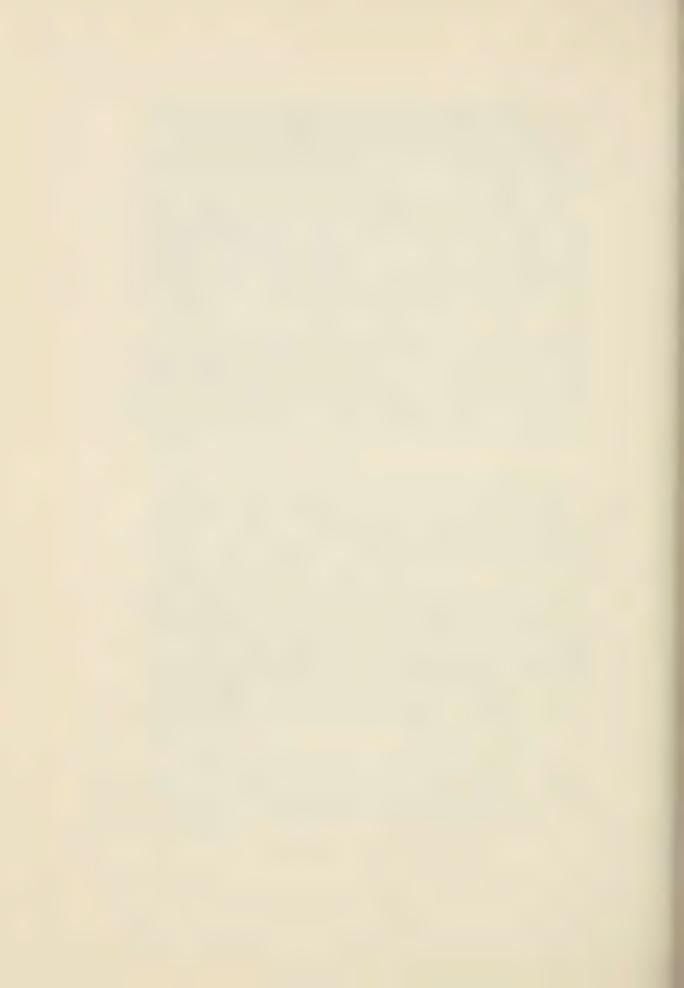
and military, for special jobs in atomic warfare. This requires a much greater degree of education and will probably be given to such people as radiological safety personnel, medical officers and civilian doctors, civil defense technicians, etc. The method by which the individual indoctrination and the specialized training is given will determine to a large extent the psychological preparation which will be attained in a population. It is highly desirable that the proper amount of knowledge be given to all so that there is created a proper respect for the special hazards of atomic warfare and that we avoid the undesirable extremes of excessive fear or ignorance. This will be a difficult job and the nation is far from attaining this ideal situation at the present time.

- g. A large amount of detailed defense planning will be required for protection of the nation. It will include large scale training of such specialists as fire fighters, evacuation control personnel, first aid personnel, and decontamination groups. Large stockpiles of food supplies, medical supplies and disaster equipment will be required in relatively invulnerable locations. Preparations will be required for mutual aid between cities and major installations.
- h. All groups, civilian and military, will need to be equipped and trained in the detection and isolation of contaminated areas. This new hazard created by nuclear radiation is the one hazard which may not be detected by any of the physical senses. It requires special instruments and special consideration.
- i. With sufficient indoctrination and a few minutes advance warning that an attack will occur, it is quite possible that a 50% saving in mortalities and casualties can be effected. This establishes the fact that development of advance detection techniques and warning signals is of the greatest importance to insure the continuation of our present existence.

II. Active Defense

i. Of less direct importance to the medical profession but of the utmost importance to the nation is active defense, which by its name means the actual prevention of an atomic attack. Regardless of our degree of preparation and protection, large numbers of casualties and a more important amount of disorganization and dislocation will occur.

- a. United Nations Organization. The attempts of the UNO to set up machinery to insure peace in the future will be by far the greatest protection we can possibly have against the atomic bomb if it is successful. We realize, however, the difficulties of getting agreement among nations which is required.
- b. Military preparedness. The basic responsibilities of military organizations require that they assume that war will occur. Otherwise they are negligent in their duties. Regardless of the political situation the military must constantly endeavor to have its preparedness kept at the highest level. In the case of atomic warfare this will consist of extensive stockpiling of all weapons, including atomic bombs. It will require readiness of retaliation forces. Because of the nature of the atomic bomb it will require extensive protection of our ability to retaliate and conduct an offensive war. As was seen above, advance warning is most important - thus an efficient foreign intelligence corps is vital. Some persons have raised the provoking thought that, because of the capabilities of the atomic bomb, we will lose an atomic war unless we attack first, assuming the enemy has atomic bombs.
- c. A vital part of active defense which is, in my opinion, erroneously played down in articles in the press is the believed futility of interception of an atomic bomb carrier and thus preventing delivery of the bomb on the target. Within the last few weeks our authorities on guided missiles have stated openly that it is their belief that guided missiles cannot be used as a carrier for at least another ten or fifteen years. The military must consider the intervening years in which it is anticipated that manned aircraft are the most likely vehicle. We have had only a fair degree of success in the interception of aircraft on bombing missions. There is no scientific reason why our degree of interception can't be raised to nearly 100% if a tremendous amount of money, time and technical ability is put on the problem. Atomic warfare, as you have seen, presents a truly horrible outlook. It is our duty to push to the utmost any procedure which could possibly reduce its effectiveness against us.



PSYCHOLOGICAL FACTORS IN ATOMIC WARFARE

James P. Cooney Colonel, M.C.

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ATOMIC WARFARE

James P. Cooney Col. M. C.

Many of the ideas I want to discuss with you today are matters of opinion -- and they are, in some cases, ideas on which the diversity of opinion seems to be a function of the number of people who have ideas. I want to talk to you about my ideas with the hope of stimulating thought and more careful consideration of a most important problem.

Please do not interpret any of my remarks as indicating anything less than the fullest respect for the phenomenon of radioactivity as a diabolical instrument of death and injury to men. I only want to point out that we are justified in taking a rather hardboiled attitude toward this subject. Since we have no choice but to live with it, we must keep it in proper perspective.

Since the advent of nuclear explosives in the so-called atom bomb, with its attendant ionizing radiations in massive amounts, unfortunate psychological reactions have developed in the minds of both the military and civilians. This reaction is one of intense fear and is directed against forces that cannot be seen, felt, or otherwise sensed. I have observed the reactions of the military, who were not acquainted with the technical details, on two missions, Bikini and Eniwetok, and the fear reaction of the uninitiated is appalling. The fear reaction of the uninitiated civilian is ever evident. It is of such magnitude that it could well interfere with an important military mission in time of war.

Whenever living cells are affected by ionizing radiation, it is detrimental. It must be realized that nature has been constantly bombarding the populations of the world with ionizing radiation since the formation of the universe - by constant exposure to cosmic radiations and to radiations emanating from natural radioactive elements - such as radon and thoron.

This kind of injury must be considered, not standing by itself, but in connection with the total situation, i.e., weighed in relation to the objectives in view, both in regard to their importance under the circumstances and their probability of attainment. Unless we can thus integrate it with our whole philosophy of national defense, the atom bomb can prove a liability rather than an asset.

With the publicity emanating from the atom bomb, the term "Roentgen" has become a household word. A Roentgen is a term of physical measurement

such as the "centimeter" or the "gram". It is based upon one of the physical effects of certain types of electromagnetic waves that cannot be measured with a yardstick. The large step from such a physical measurement to expected biological behavior in humans is based upon experimentation on lower animals, empirical observations, and clinical investigations. There are, however, many blank spaces in our experience and many superstitutions have been introduced. Since it is impossible to stipulate all conditions of experimentation and observation in most of the articles written about radiation for lay consumption, an idea has evolved in many minds that any and all radiation exposure will cause immediate and mysterious injury or death. This reasoning is fallacious, but it is also attractive and has become contagious.

The problem of radiation injury is not one which can be easily simplified. In fact, over-simplification of this danger may be the cause of a situation such as we are combatting at this time. It seems desirable to explore radiation hazards more fully in relation to other hazards which are considered more common and acceptable.

The permissible radiation dose is 0.2 or 0.1 r per day, or 0:3 r per week according to your authority. It should no longer be called the "tolerance dose" for no amount of radiation should be tolerated without good reason. One is willing, however, to name a dose so small that a person might be exposed to it every day of his life and suffer no observable injury nor shortening of his life span.

When one is dealing with radiation technicians or with industrial workers who are exposed to this hazard daily in their life's work, one can easily see how the maintenance of exposures at or below this level is a very desirable thing. Day by day contact with radiation or radioactive materials demands that a low limit of exposure be adhered to, if one is to avoid late complications of such chronic trauma. Similar occupational hazards exist in all branches of production --- noxious gases and dust to the coal miner, the steel worker and the chemical worker. It has been known for years that if a miner is subjected to small amounts of dust containing silica that he eventually will develop silicosis, frequently complicated by tuberculosis, and a fatal termination. For this reason, methods of counting and analyzing dust have been perfected, and forced ventilation systems have been established to minimize the danger. This does not mean that if an individual makes a one day visit to a mine and inhales 100 times the daily minimal allowance for miners that he will develop silicosis. This tolerance limit has nothing in its definition which refers to acute exposure. Neither is the 0.1 r per day tolerance limit related to acute exposure in radiation.

The total body dose of radiation received as an acute exposure is known from the rapeutic experience to vary with the patient. This and the lethal dose for man have not received the same attention from

rule-making bodies that the "permissible dose" has had. We may take 450 r as the median lethal dose.

Going further down the scale, one may consider a limit of 200 r, which may cause radiation sickness in 50 percent of human subjects when delivered, as an acute dose of total body radiation. Some subjects may be quite sensitive to radiation and others quite resistant, so it is difficult to calculate the precise effects to be expected.

It is not unusual to subject a patient to multiple X-rays of the skull, spine, long bones, gastro-intestinal tract, kidneys, sinuses, etc. in a relatively short space of time, thus subjecting him to a dose of radiation which may well approach 25 r. These procedures are not done without purpose and the benefit from the information gained outweighs all fear as to the possible injury from radiation. Full body radiation in doses of the order of 25 r to 100 r have been given to patients for treatment of various conditions. Again these exposures are prescribed for a purpose which outweighs the fear of radiation injury.

It is not the purpose of this article to underestimate or understate the radiation hazard. But from a military standpoint the physical danger must be evaluated against the objective to be gained.

War is fought with the knowledge that men will be killed. Campaigns are planned with expectation of losing so many thousand men. If you call these "acceptable hazards" then it is obviously not wise to treat radiation hazards very much differently. If acceptance of radiation hazard will lessen the other military hazards, then that is what one should accept. This can only be done, however, if the attitude of the men exposed is psychologically similar toward the two types of hazards. If they are going to be as much terrified by the knowledge that a recent atom bomb explosion has contaminated the ground they are walking over as they would be by seeing one in ten of their buddies fall by machine gun fire, one cannot apply the "ideal" solution. What is dominant for actual percentage survival is the resultant of all the actual hazards. But for battle discipline and military effectiveness the dominant measure is not the hazard itself but the soldiers' estimation of the hazard.

Men at war suffer many hazards, acute and chronic, besides bullets; malaria, veneral disease, exposure to cold and wet, starvation, etc. Some of these, e.g., VD, are underevaluated by the doughboy. Others, e.g., filariasis, are grossly over-evaluated. At present radiation is perhaps over-evaluated worst of all, partly due to our great care in Operations Crossroads. That operation was conducted at the peace time level of safety to personnel. Unless we had openly proclaimed immediate danger of war, the military level for hazardous training programs, such as we had actually adopted during the war, using live grenades and live ammunition in the machine guns, was not tolerable at Bikini. It must be emphasized that acceptable hazards in a peace time operation, cannot be adhered to in war time.

Psychological training for the military level of acceptable radiation hazard is possible and should be prosecuted, even though operation field training does not permit this to be accomplished at the present time.

We hear much about sterility as a result of exposure to ionizing radiation. It must be borne in mind that sterility results only from a large dose of acute radiation, or from smaller doses over a long period of time - a matter of years. Sterility also results from other accepted hazards encountered in war - Veneral disease is one of the foremost causes of sterility. We are aware of hundreds of paraplegies resulting from spinal fractures, gun shot wounds of the cord, etc., during the last war who are not only sterile but impotent. Leukemia may be another late result in casualties from repeated radiation, but amoebic dysentery and schistonomiasis carry a great delayed hazard, and so does the effect of beri-beri, which was so prevalent among our prisoners-of-war.

I have knowledge of a death at Bikini caused by drinking wood alcohol. There were other deaths due to various types of accidents. At Eniwetok we had a death due to drowning; one due to a truck accident, and one due to a fracture of the skull encountered in a fight. A sailor sustained a fracture of the cervical spine with severence of the cord by diving into shallow water. He will be paralyzed, sterile and impotent as long as he lives. None of the above tragic deaths received national news publicity. However, had we had a single death due to radiation, would it have been publicized? It would have received front page publicity throughout the country.

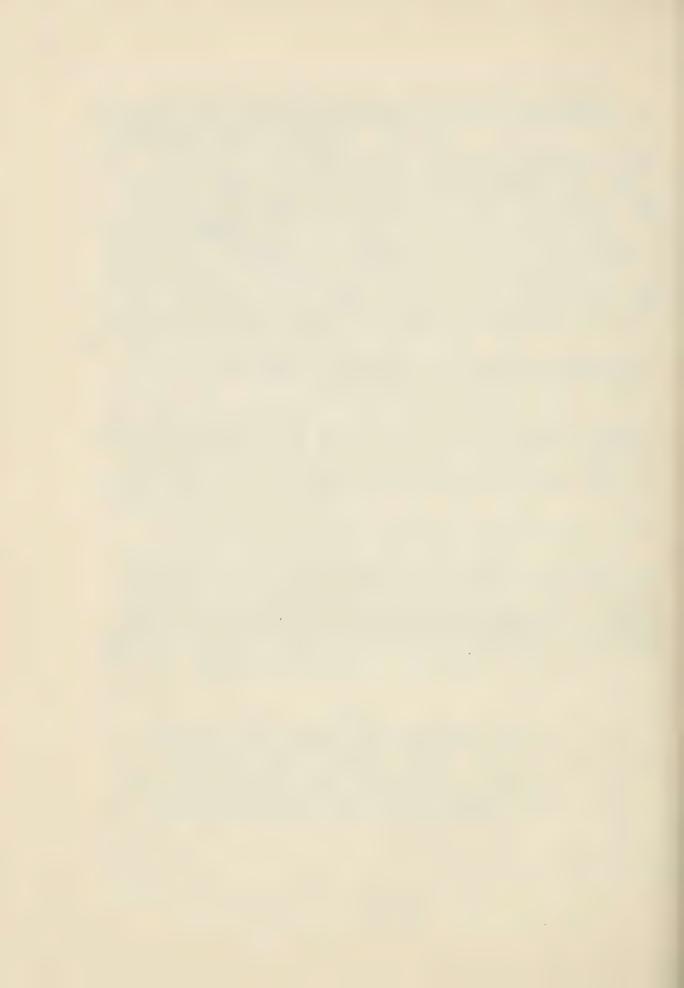
During August of 1946 I interviewed and examined a large number of Japanese who had recovered from radiation sickness. They appeared perfectly hormal and were handicapped in no way toward pursuing their way of living. Such is not the case with thousands of our soldiers who participated in "conventional" warfare in World War II. They are handicapped by loss of limbs and eyes. Neither is it true of many of the Japanese who received no radiation injury but received severe burns and traumatic injury as a result of the bombing. It has been estimated that from 5 to 15 percent of the deaths at Hiroshima and Nagasaki were due to radiation. Why do we concentrate on the 15 percent and forget the 85 percent?

The atomic bomb was developed as a blast weapon of war and strategically so used. The radiation effect was never considered to be the
prime component of its effectiveness. The destruction attendant to the
blast, heat and secondary fires was paramount. In Japan there was no
significant "poisoning" of the ground by fission products or induced
activity from neutron capture, and yet many believe that the bomb is
primarily a weapon which destroys by mysterious radioactivity.

I have appeared before local defense agencies in many of our cities. They are preparing for defense against an atomic bomb attack - universally they are thinking only of radiation. Invariably they ask, "Where will we get Geiger counters? Geiger counters are not their only problem - firefighting equipment is many times more important, as well-organized rescue squads. "But we have been told that we will not be able to go into a bombed city and rescue the injured." Hiroshima and Nagasaki disprove this. The residual radiation from an air burst bomb is insignificant. The significant prompt radiation occurs in a matter of microseconds and does not extend beyond a 2000 yard distance. Immediately after such a detonation, such as Hiroshima or Nagasaki, it is perfectly safe to enter a bombed area and rescue the thousands whose injuries will be such that they will not be able to walk. Unless evacuation of these injured is effected, thousands will be burned to death by secondary fires. Such was the case at Hiroshima and Nagasaki. But how about an underwater or ground burst? In such cases certainly the residual radiation hazards would be increased many fold, but the blast and fire hazards and the prompt radiation hazard would be proportionately decreased, and in my opinion, the total number of casualties would be less.

If we are to live with this piece of ordnance and ever have to use it again in the defense of our way of living, we must acquire a practical attitude, not only toward its efficiency or limitations as a bomb, but also toward the possible effects and limitations of this "mysterious" radiation. We must recognize that the casualties caused by the blast and burns from this weapon will be many times greater than the deaths caused by radiation. We must also dispel the erroneous idea that the rescue work of the injured will be impossible due to residual radiation.

It is of the utmost importance that we recognize that the radiation hazards are additional hazards. They only add to the complexity and perhaps even the severity of the other hazards of total warfare. Therefore, we must not and cannot concentrate on this phase of atomic warfare to the detriment of other defensive preparations. Rather, we must know and understand the facts about ionizing radiations if we are to survive the other dangers.



THE

PRODUCTION, PROCUREMENT, AND HANDLING

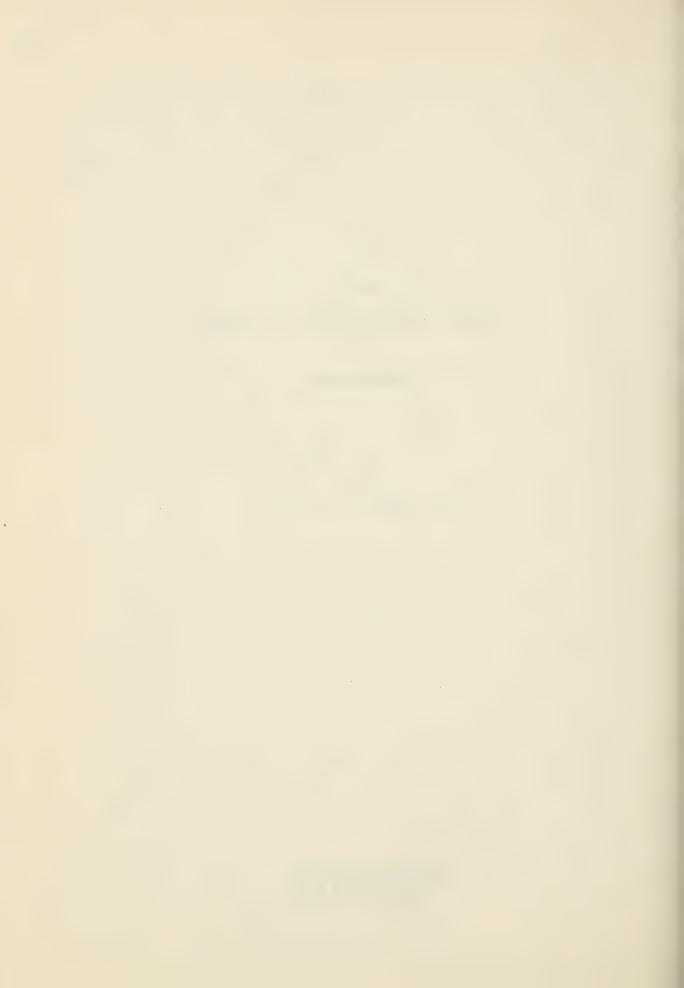
OF

RADIOISOTOPES

By

Major Maxwell Dauer, MSC

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THE PRODUCTION, PROCURELENT AND HANDLING OF RALIOISOTOPES

by
Major Maxwell Dauer, MSC

Introduction

The artificial production of radioisotores for scientific use dates back about 14 years. However, the radioactive elements that occur in nature were used as sources of radiation, and even as tracers, virtually from the time of their discovery during the early years of this century. The first tracer experiment was conducted by Hevesy in 1912 who demonstrated that radium-D was chemically the same as lead.

Most of the naturally occurring radioisotopes belong to the heavy elements between thallium and uranium. There are four relatively light natural radioactive elements, which include potassium, rubidium, samarium, and lutecium. None of these enter much, if at all, into life processes. Therefore, few biological tracer experiments were performed with the natural radioisotopes. The primary use was for radium and its associated elements as a therapeutic agent.

In 1934, the Joliet-Curies discovered that radioactive isotopes of the naturally stable elements could be produced by nuclear bombardment. Within a few years, cyclotrons and other particle accelerators had produced radioisotopes of all of the stable elements. By 1940, some 370 varieties were known.

As soon as radioisotopes of carbon, phosphorus, sulfur, iron, iodine, and other elements entering into life processes became available investigators put them to work. It was tremendously costly to produce isotopes in cyclotrons. However, their value as research tools was unique and the effort to produce them with cyclotrons was justified.

The wartime development of the atomic pile made possible the widespread use of radioisotopes in hitherto undreamed of quantities. The production of about 200 millicuries of carbon 14 in a period of a few weeks at the Oak Ridge pile, theoretically would require about one thousand cyclotrons to equal this output. Almost a year after the first use of the atomic bomb, the first shipment of radioisotopes was made from Oak Ridge. By late 1947, the increased supply of radioisotopes permitted allocations for research in all fields.

The production of radioisotopes is dependent primarily upon the pile facilities of the Atomic Energy Commission and to a minor extent on particle accelerators. The procurement of radioisotopes from the Atomic Energy Commission must conform to certain procedures which will be described. The widespread use of radioisotopes introduces a requirement for precaution in order to avoid the hazards of these radioactive materials.

Cyclotron Production of Radioisotopes

The two outstanding instruments for the production of radioisotopes are the chain reacting pile and the cyclotron. Versatility in isotope production is the outstanding feature of the cycletron. There are other particle accelerators which may be used for isotope production. However, the cyclotron, at present, is the principal apparatus together with the pile for the production of radioisotepes. The number of particle accelerators - cyclotrons, synchrotons, betatrons, linear accelerators, etc., in operation in about 50 U.S. laboratories will be doubled by construction already scheduled. At least two dozen of the new atom smashers will be capable of bombarding the nucleus with particles accelerated to more than 100 million volts. The giant 184 inch synchrocyclotron at the Radiation Laboratory of the University of California, Berkeley, is the world's greatest at this time. A proton synchrotron is being constructed at Brookhaven National Laboratory to yield protons with energies between two and three billion electron volts (Bev). A similar machine is being constructed at Berkeley to yield protons with energies between six and seven Bev.

The essential component of the cyclotron consists of two short, hollow, half cylinders, called dees. The dees are mounted inside a vacuum chamber between the poles of a powerful electromagnet and connected externally to a high frequency alternating current generator. When a trace of hydrogen gas is introduced into the evacuated chamber, a het wire filament ionizes some of the hydrogen atoms producing the protons. By alternating the charges on the dees, the protons move through the strong magnetic field of the huge magnet in a circular pattern. As the petential reverses periodically in the dees, the proton travels faster and faster moving in ever expanding circles until it passes out through a narrow open window. In this manner the beam is used to bombard various substances which are studied by various means of detecting devices. Perhaps the most interesting fundamental principle that makes the cyclotron work at all is the fact that the time required for charged particles to make half the turn within the dees is the same for all speeds. The faster a particle travels, the larger is the circle it must travel, thus keeping the time constant. Hence, with a constant frequency with an alternating current supply, some particles may be just starting to move while others farther out may be moving with higher speeds.

When the hydrogen in the evacuated chamber in the cycletron is replaced by deuterium, a beam of high energy deuterons is obtained. If helium gas is used in place of deuterons, many of the atoms become doubly ienized in the cycletrons and thus emerge from the cycletron window with an energy double that of the deuterons and protons. By increasing or decreasing the frequency of the petential applied to the dees and properly adjusting the magnetic field, various emergies of protons, deuterons, or alpha particles of 1 Mev and up become available.

Cycletren targets are bembarded in two locations; in the external beam and on a probe. By deflecting the deuteron beam out of its last circle in the cycletron chamber by means of a high negative potential on a deflector electrode, the beam can be made to pass through a thin aluminum alley window at the side of the vacuum chamber. With a suitable external target chamber low melting or volatile materials such as sedium, red phosphorus, or salts can be bembarded on water-cooled plates in an inert gas atmosphere, such as helium. Because only a fraction of the total number of ions accelerated can be directed into an external beam, the production efficiency of this method of bembardment is comparatively low.

In utilizing the probe for bombardments, the problem of power dissipation seriously limits this method. Here the target material is fastened to a water cooled target head and inserted into the vacuum chamber to a point nearer the middle of the gap between the end of the does. In this location, the target intercepts the circulating ion beam in its final circle of the chamber. In order to spread the beam over a large area, the target head is bent so the beam hits the target at a small angle. The bombarded area is still further increased by making the target head oscillate. When using probe targets, such as a cobalt-copper telluride for making I-130, more than half of the activity is lost by volatilization.

The yields of isotopes by cyclotron production depend upon beam current, voltage, and fraction of target element in the target material. Of course, the yield decreases with volatilization of the product and target.

If the cycletron target is beryllium metal, a high yield of neutrons from the reaction

$$4^{B 9} + 1^{H^2} 5^{B^{10}} + 0^{n^1}$$

is obtained. For 14 Mev deuterons, these neutrons have a maximum energy of 18 Mev and a high flux of fast neutrons exist directly behind the target.

The cyclotron is able to produce all the synthetic radioisotopes which are known. Table 1 lists some of the cyclotron produced radioisotopes.

Pile Preduction of Radioisotopes

There are three ways in which neutrons in the pile produce radieisotopes: (1) by splitting atoms of fissionable uranium into new
atoms of entirely different elements -- fission products, so-called -which are radioactive themselves; (2) by being captured in the nuclei
of atoms of special "target material" inserted into the pile, turning
them into heavier isotopes of the same element; (3) by altering the
electrical charge of the nuclei of atoms of target material, thereby
transmuting them into isotopes of a different element.

Uranium fission products removed from the pile centain a great variety of radioactive materials, which -- in method (1) above -- can be extracted and purified by chemical means. However, the radio-isotopes obtained are all those of elements near the center of the atomic scale between zinc (30) and gadelinium (64). With the exception of iodine 131, those do not now enter significantly into medical, biological, agricultural, or most industrial processes. Therefore, most of the radioisotopes supplied by Oak Ridge must be prepared by methods (2) and (3). These call for the preparation and pile irradiation of special target materials. Phosphorus 32, a widely used radio-isotope, can be produced by both methods and may be used to illustrate.

In the production of phosphorus 32 by "neutron capture," method (2), phosphorus 31, contained in phosphate, is put into aluminum cans which are set in holes in a graphite block and pushed into the center of the pile. Each atom of the stable element phosphorus 31 that captures a neutron becomes phosphorus 32. But not enough neutrons are present in "low flux" piles to convert more than a small propertion of the phosphorus atoms to the radioactive state. Hence the phosphorus 32 is still much diluted with phosphorus 31, and the treated phosphate is not highly radioactive.

In practice, therefore, phosphorus 32 is usually produced by method (3), "transmutation." This process starts with a target element different from the element of which an isotope is desired. Sulfur is the target for the production of phosphorus 32. Bembardment by neutrons in the pile changes the electrical charge of the nuclei of some of the sulfur atoms, and thus transmutes them into phosphorus 32. When the sample has been removed from the pile, the radioactive phosphorus can be chemically separated from the target sulfur. Phosphorus 32 in a very pure form, high in radioactivity, can thus be obtained. Unfortunately many important radioisotopes — those of calcium, iron, and zinc, for instance — cannot effectively be made by transmutation. They can be produced only by neutron capture, and this, as stated above, gives a product low in radioactivity.

When a pile of higher neutron flux becomes available, it will be possible to produce radioisotopes of greater usefulness for research.

From the preparation of the target material to the final shipment of the product, the production of radioisotopes demands skilled personnel and special equipment. When the pile is shut down for the removal of the irradiated samples, each member of the team of workers must know precisely his assignment in the operation and carry it out quickly and without error. Geiger counters and other radiation detection equipment must be used constantly to check the radiation present. In subsequent chemical treatment of materials, the work must be carried on behind lead shields, the workers using tongs and mirrors to avoid exposure. Many chemical operations are conducted inside a "hot lab," a room with thick concrete walls in which apparatus is manipulated from outside by remete control devices, the chemist viewing his work through periscopes. Each radioisotope, moreover, is a separate production problem, involving its own combination of requirements -- for target material, irradiation time, chemical treatment. safety precautions, and the rigid time limits associated with its inflexible half-life.

Table 2 includes some of the more important pile isotopes useful in biological and medical sciences.

Procurement of Radioisotopes

The program for the distribution of pile-produced isotopes was formulated with the assistance of the best scientific advice obtainable. Early in 1946, at the request of the Manhattan Project, the president of the National Academy of Sciences nominated a panel of distinguished scientists from which an interim Advisory Committee on Isotope Distribution Policy was formed with two members experienced in each of the major fields of isotope application. This group was largely responsible for establishing the policies that have guided the distribution program since its inception.

Originally, radioisotopes were allocated in the following order of priority: (1) for publishable research in the fundamental sciences, including human tracer applications, requiring relatively small samples; (2) for therapeutic, diagnostic, and tracer applications in human beings and publishable research in the fundamental sciences requiring larger samples; (3) for training and education by accredited institutions in the techniques and applications of radioisotopes; and (4) for publishable research in the applied sciences, including industrial research. Now, however, production has increased to the point where it is not necessary to apply priorities to the distribution of the more important isotopes. Radioisotopes are made available to individuals only through institutions that have the personnel and equipment to handle them usefully and safely. Secondary distribution is not permitted without specific authorization.

At present 100 kinds of available radioisotopes are listed and described in the AEC Catalogue and Price List issued by the Isotopes Division. New prospective purchasers submit an application describing the research they propose and their facilities for radiation measurement and health safety monitoring, and agree to publish the results of their investigations. Applications are reviewed by scientists in the Isotopes Division and if necessary by the Subcommittee on General Applications and by the Subcommittee on Human Applications when such use is contemplated. In the two years of the project's operation 1,742 applications have been received and 1,700 approved.

By the end of June 1948, 3,136 shipments of pile-produced radioisotopes had been sent from Oak Ridge to users outside the Commission
in 33 states of the United States, the District of Columbia, and Hawaii,
The recipients were 236 institutions: 54 medical organizations and
hospitals, 111 educational institutions, 53 industrial organizations,
and 18 public and private nonprofit research institutions. Within
these institutions more than 385 different departments are using radioisotopes.

Shipping of Radioactive Materials

The widespread use of radioisotopes and their shipment to various laboratories has been a serious problem. In order to provide adequate protection, the Interstate Commerce Commission premulgated regulations for controlling shipment of radioactive materials. The most pertinent points of this regulation* are abstracted below.

1. Radioactive Materials:

- a. Group I. Radioactive materials that emit gamma rays only or gamma rays and alpha and/or beta rays.
- b. Group II. Radioactive materials that emit neutrons only or neutrons and alpha, beta and/or gamma rays.
- c. Group III. Radioactive materials that emit alpha or beta rays only.

2. Packaging and Shielding Requirements:

- a. Radium, plutonium or strontium must be packed in an inner metal centainer of stainless steel, malleable iron or brass, not more than 3 in. in diameter or 8 in. in length, minimum wall thickness 1/8 in. and having screw closure.
- b. Fogging of undeveloped film at 15 ft for 24 hr must not exceed that produced by 11.5 mr of gamma rays of radium filtered by 1/2 in. of lead.

^{*}Federal Register, Vol 12, No. 220, pages 7329 - 7333.

- d. Outside container must be of such design that gamma radiation will not exceed 200 mr/hr at surface.
- e. Group I radioactive materials must be so packed and shielded that gamma radiation at one meter (39.3 in.) from radioactive source does not exceed 10 mr/hr.
- f. Group III radioactive materials must be so shielded and packed as to prevent the escape of primary alpha or beta radiation, and secondary radiation at the surface of the package must not exceed 0.4 mr/hr (10 mr/24 hr).
- g. Liquid radioactive materials must be surrounded by absorbent material which will completely absorb liquid in case of breakage. Materials packed in metal tube do not require absorbent packing.

3. Labels:

- a. Each outside container of Group I or II radioactive materials must carry the special red on white label with certification.
- b. Each outside container of Group III radioactive materials must carry the special blue on white label with certification.

4. Exemptions:

Radioactive material that meets all of the following conditions is exempt from prescribed packaging, marking and labeling requirements:

- a. Package must be such that there can be no leakage during normal transportation.
- b. Package must contain not more than:

(1) 0.1 mc of radium or polonium

(2) That amount of Sr^{89} , Sr^{90} or Ba^{140} which disintegrates at a rate of more than 5×10^6 atoms/sec (0.13 mc).

- (3) That amount of any other radioactive substance which disintegrates at a rate of more than 50 x 10⁶ atoms/sec (1.3 mc).
- c. Package must be such that no significant alpha, beta er neutron radiation is emitted at the surface of the package and the gamma radiation at any surface must be less than 0.4 mr/hr (10 mr/24 hr).

Personnel handling radioisotopes must take adequate steps to prevent exposure to high intensities of radiation. Likewise, equipment and facilities must be properly designed to provide protection for laboratory personnel and minimize radioactive contamination. The amount of external radiation not in excess of 100 millirems per day has been generally accepted as the permissible exposure.

Every worker with radioactive materials is exposed to potential personal danger from two directions. The first is from radiation external to the body, and originating from the source, from contamination outside the source container, or from contamination of one's clothes or person. The second is from internal radiation originating from the inhalation of radioactive material, from the ingestion of radioactive material, or from radioactively contaminated wounds. When the external radiation hazard is not significant, the problem reduces to that of maintaining a radiochemically "aspetic" technique and is similar in principle to that met in handling infectious bacteria.

Contamination problems are, in general, a function of the half-life of the radioisotope which is involved, while the radiation health hazard is dependent upon the amount and energy of the activity present. For example, both sodium 24 (14.8 hr half-life, 1.4 Mev beta, 1.4 and 2.8 Mev gamma) and potassium 42 (12.4 hr half-life, 75% 3.58 Mev beta, 25% 2.07 Mev beta, and 1.51 Mev gamma) present substantial health hazards in millicurie amounts since they emit high energy beta and gamma radiations but only minor contamination hazards since they have short half-lives. On the other hand, when working with high millicurie strengths of a pure beta emitter with a long half-life (for example, Ca 45, 180 day half-life, 0.3 Mev beta), the health hazard of external radiation will be small while the contamination hazard is considerable.

There are listed some general rules for handling beta and gamma emitters in a typical "hot" laboratory:

- 1. No person should enter a "hot" laboratory unless he has a reason to be there. Visitors especially should be limited.
- 2. Laboratory coats usually worn in the "cold" laboratory should be removed before entering the "hot" laboratory.
- 3. All persons working in the "hot" laboratory should wear a laboratory coat; such coat to be kept and worn in "hot" laboratory only.
- 4. Each person should monitor bench top, apparatus and material with which he is working before and after completion of the work. Meter readings are to be recorded in the "hot" laboratory notebook. The following tolerance

levels of radioactive contamination should not be exceeded:

Shoes

1000 counts per minute (cpm)

Laboratory coats and clothing

500 cpm

Table tops, floors, etc.

300 cpm with counter in

contact

Inside intermittently used hood

Zero cpm

Smear test on table tops, floors, apparatus, etc. (2 sq in. filter paper smeared over 12 sq in. and checked with a counter)

Boxes for shipment by air or mail

Zero cpm with smear test.

Total radiation at outside surface of box in accordance with Interstate Commerce Commission Regulations.

All laboratory and operating areas

All areas with radiation greater than 12.5 mr/hr should be posted.

- 5. Before leaving "hot" laboratory, hands should be monitored and scrupulously cleaned until smear tests yield a reading of zero. Under no circumstances should direct readings on the hands exceed 700 cpm. If it is not possible to reduce the activity to this degree, a responsible individual within the laboratory should be informed immediately.
- 6. No work should be done on bench tops unless absorbent paper is first laid down.
- 7. When work is completed, each person should individually clean and/or dispose of contaminated material.
- 8. Activity should be disposed of in waste jars kept in each sink; paper towels should be disposed of in special containers, etc.
- 9. The "hot" laboratory should receive a general clean-up and monitoring the last day of each week.
- 10. All unused activities should be kept in the "hot" laboratory safe. The removal of any activity should be done early with the approval of a responsible individual within the laboratory.

- 11. All activities entering or leaving the "hot" laboratory -for shipping, for use in a "cold" laboratory, or for any
 other reason -- should be monitored and a dated and
 initialed record entered in the "hot" laboratory log book.
- 12. No Smoking, Eating or Drinking should be permitted in the "hot" laboratory at any time.

Disposal of Radioactive Wastes

With an expansion of the radioisotope distribution program of the AEC, it is becoming increasingly apparent that some guides must be established for the proper disposal of waste radioisotopes. There has been no general agreement, as yet, regarding the recommended practices for waste disposal. Nevertheless, the following suggestions are offered:

- 1. Radioisotopes having half-lives of less than 30 days may be disposed of in the sewer, provided the daily volume of water flowing through the particular outlet used is sufficient to dilute the radioisotope to 0.1 microcuries per liter or to safe limits of concentration as set for that particular isotope. This practice should be contingent on certain provisions such as:
 - a. The maximum activity disposed of in any one institution should not exceed 100 mc. per week.
 - b. Regular radiation surveys of the plumbing fixtures.
 - c. Appropriate surveys before repairing the plumbing between the disposal outlet and the main sewer.
- 2. Radioisotopes of any half-life may be buried in the earth, provided that they are uniformly diluted with stable isotopes of the same element to the extent that 4.15 ergs (equivalent to 50 mr/day in tissue) is dissipated per gram of element per day, provided:
 - a. The burial is made only in suitably selected areas which are in possession of and will be maintained by the user. These areas should be properly marked and enclosed with suitable fencing. In case of possible release into the soil, a thorough geological investigation should be made of the area selected for burial purposes, and analyses should be provided of the soil, so that the fate of the material can be determined to be a safe dilution.

- b. The material should be buried at a minimum depth of 5 feet.
- 3. Radioactive materials may be buried when properly enclosed in a container sufficiently well constructed to retain the isotope for a period of five years, provided:
 - a. For materials having half-lives of 2 years, the radioisotope is adulterated, prior to enclosure, with
 sufficient quantities of concrete or stable isotopes
 of the same element to reduce the dissipation of energy
 from the remaining activity at the end of 5 years to 4.15
 ergs per gram of adulterant. The dosage rate at the surface of the container shall not exceed 6.25 mr/hr.
 - b. For materials having half-lives of 2 years, the radioisotope should be adulterated, prior to enclosure, with sufficient quantities of concrete or stable isotope to reduce the dissipation of energy to the extent of 4.15 ergs per gram of adulterant per day.
 - c. The burial is made in compliance with 2a above.
- 4. Materials may be buried at sea when enclosed under conditions stated in 3 above and buried beyond the three-mile limit.
- 5. Materials containing radioisotopes may be incinerated if the calculations of safe permissible concentration in exhaust air and in disposed ashes are based on known values. In the absence of specific information, the following assumptions should be made:
 - a. For the air calculation, that all the active material escapes in the air.
 - b. For the handling of the ashes, that all the activity is retained in the ashes. The ashes and/or effluent residue are then disposed of in accordance with 2 and 3.

Some cyclotron produced radioactive isotopes of interest

Isotope	Half-life	Production reaction	Bombardment location	Criteria* for listing
Be ⁷	43d	Li(d,n)	Ext	а
cl1 F18	20.5m 112m	B (d,n) O (d,n)	Probe. Ext Ext	b a
Na 22	3.0y	Mg (d,a)	Probe. Ext Probe.	ъ
Si ³¹ Cl ³⁸	170m 37m	Si (d,n) Cl (d,p)	Ext Ext	d d
Mn52 Mn54 Fe55	6.5d 310d 4y	Cr (d,2n) Fe (d,a) Mn (d,2n)	Probe.	b b
Fe59	44d	Co (n,p) (fast neu-	Probe.	be be
56	85d	tron).		
57 Co ⁵⁸	270d 65d	Fe (d,n) (d,2n)	Probe.	ъ
Zn ⁶⁵ As ⁷⁴	250d 16d	Cu (d,2n) Ge (d,2n)	Probe.	Ъ
Se ⁷⁵ Kr(^{79,81})	115d 34h	As (d,2n) Br (d,2n)	Probe.	b
Xel27 1130	34d 12.6h	I (d,2n) Te (d,2n)	Ext	ъ
Hg197	23h 64h	Au (d,2n)	Probe.	Ъ

^{*}Criteria for listing: (a) available only by bombardment with high energy positive ions, (b) carrier-free isotopes of these elements available from the cyclotron, (c) isotopically pure products best obtained with the cyclotron, (d) important isotopes with half-lives too short to use away from the source of production.

Table 2

Pile Produced Isotopes Especially Useful in the Biological and Medical Sciences

Isotope	Half-Life	Reaction
C 14	5100 ***	n nuctuu
Na 24	5100 yr 14.8 hr	n, proton
P 32		n, gamma
	14.3 d	n, proton
S 35	87 d 10 ⁶ hr	n, proton
C1 36		n, gamma
A 37	34 d	n, alpha
K 42	12.4 hr	n, gamma
Ca 45	180 d	n, proton
Fe 55		n, gamma
Fe 59		n, gamma
Co 60	5.3 yr	n, gamma
Ni 59	15 yr	n, gamma
Cu 64	12.8 hr	n, gamma
Zn 65	250 d	n, gamma
As 76	26.8 hr	n, gamma
As 77	40 hr	daughter of n,
		gamma Ge77
Br 82	34 hr	n, gamma
Rb 86	19.5 d	n, gamma
Sr 89	53 d	fission products
		mixture only
Sr 90	25 yr	fission products
	•	mixture only
Mo 99	67 hr	n, gamma
Ag 110	225 d	n, gamma
Ag 111	7.5 d	n, gamma
Sb 122	2.8 d	n, gamma, mixture only
Sb 124	60 d	n, gamma, mixture only
Sb 125	2.7 yr	daughter of n, gamma
		Sn 125
I 131	8 d	fission product or
		daughter of n, gamma
		Te 131
		x 0 x 0 x

References

Aebersold, Paul, Isotopes and their application to peace time use of atomic energy. Bulletin of Atomic Scientists, 154 - 158, May 1948.

Rules and procedures concerning radioactive substances and associated hazards. AEC, February 1947.

Fourth Semiannual Report, AEC, 1948.

Woodruff, N. H., and Lough, S. A., Preparation and procurement of radioactive materials, Nucleonics 3, No. 2, August 1948.

Lawrence, J. H. and J. G. Hamilton, Advances in Biological and Medical Physics, Academic Press, 1948.

Availability of radioisotopes, Chemical and Engineering News 26, p. 2260, August 2, 1948.

Morgan, K. Z., Shipping of radioisotopes, Journal of Applied Physics 19, p. 593 - 598, July 1948.

Woodyard, J. R., High-energy particle accelerators, Electrical Engineer 67, p. 759 - 767, August 1948.

Brown, D. F., Health aspects of radioactive work. Proceedings of Conference of Nuclear Chemistry, Chemical Institute of Canada 205-211, 1947.

Levy, H. A., Design of radiochemical laboratories. Chemical Engineering News, 24, 3168 (1946).

Nemiques, F. C., and Schreiber, A. P., Administration and operation of a radiochemical laboratory, Nucleonics, p. 1 - 4, March 1948.

PUBLIC HEALTH ASPECTS OF ATOMIC ENERGY

By

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Public Health is that branch of medicine which deals with the relationships between individuals and the community. The concept of public health is fluid and changing. There was the "Hygienic" era with its abolition of the roller towel; the "Prophylactic" era, so well known to military men and those of the dental profession. At the present time the emphasis is shifting from the negative - absence of disease - to he positive, presence of health.

Through it all permeates the philosophy of a general bonification of the environment in which we live. The mere vastness of the field carries with it the danger of loss of perspective. This leads to the expanding of undue effort on relatively unimportant aspects at the expense of those which should have priority. A retention of perspective becomes increasingly necessary in warfare or other widespread emergencies.

Assessment of Hazard

You as medical officers will be called upon to assess the hazard and to advise the command accordingly. You will probably have the necessary physical findings supplied to you. The presence or the magnitude of the hazard will depend upon many factors. You will frequently need the advice of not only the physicist (Engineer Corps or other specially trained line officer) but also of such disciplines as meteorology, geology and hygrography. In damp or rainy weather there is little dust; therefore, ground contamination will not be as serious from an internal (inhalation) standpoint as during dry conditions.

In assessing the hazard, keep ever in mind that external radiation is more easily dealt with than internal radiation. You can guard against external radiation, but you must prevent internal radiation. Decontamination of the skin, though at times difficult, is far easier than decontamination of the liver, lungs or bone.

Personnel monitoring devices are of many kinds. Most usual at the moment are:

- a. Film meters
- b. Pocket ionization chambers
- c. Pocket electroscopes.
- d. Geiger-Mueller tubes.

Area monitoring instruments include:

- a. Geiger-Mueller tubes.
- b. Electroscopes.
- c. Ionization chambers.
- d. Film meters
- e. Dust or air sampling devices.

Let us assume that an area is contaminated. It may be contaminated with:

- a. Alpha emitters. This will constitute a most serious hazard if such substances gain access to the interior of the body. There will be no external radiation hazard.
- b. Beta emitters. This will constitute both external and internal radiation hazard more serious per unit if internal.
- c. Gamma emitters. Here again we must think of both external and internal hazards, more serious from a practical standpoint as an external hazard.
- d. Combination. Contamination will almost certainly not be limited to one of the above types of radiation.

Advice as to Eating Food In Contaminated Area

It must be assumed that all food found in the area is dangerous. The food may contain induced radioactivity. This is unlikely to be present in dangerous quantities because of generally unfavorable reactions, and because of short half-life of many substances. You as medical or veterinary officers will, however, probably be called upon to give an opinion in these cases.

The food may have deposited radioactivity on its surface and this is most likely to be the case. Here, as in many cases, decontamination will be impractical or impossible. Canned or otherwise protected foods may be eaten only after careful inspection and most rigorous and wise attention to detail of removing the food from the protecting agent.

If it is necessary to bring food into the area, a high degree of precision must be maintained in the handling of it.

Livestock

A serious food supply situation may arise as a result of bombing near large stock yards. Let us assume that the stock, be it cattle, sheep, swine or other, has probably received a lethal amount of radiation but that many have survived the blast effect. Let us further assume that there has been no appreciable fall-out, and that we are in the area shortly after the detonation. We are therefore dealing with animals suffering from external irradiation. To be sure there will be some induced radioactivity but this will be of so small an amount as to be negligible. The animals could therefore be slaughtered and the meat saved for food. This along

with all operations in the area must of course be carried on under the surveillance of the radiological defense or safety group. If the area is contaminated and the stock has been eating contaminated food for a few days, the picture is considerably more complicated. Hides and viscera will be contaminated and should be removed and handled in such a way as not to contaminate the meat. Meat must be carefully examined for radioactivity and discarded if more than a trace is found. If time is available and other conditions permit, it may be well to consider moving the stock to non-contaminated areas and feed on non-contaminated food. The physical and biological half-life will lead to less highly contaminated animals and the shifting of elements during metabolism will shunt most of the more harmful elements away from the muscle. In contemplating such a move, the feasibility of properly handling contaminated excreta and slaughter house offal must be considered. It is reasonable to expect milk produced by an internally contaminated cow to contain radioactive elements. Here one must be guided by the facts as they present themselves. If the milk is contaminated, centrifuge and test the cream and skimmed milk separately. If only one portion is contaminated, the other portion may be used as food. If both are contaminated, the degree of contamination must be weighed against the need for the food. Remember that field detecting instruments were not designed for this purpose and a low reading may indicate serious contamination. Contaminated hides, excreta, and slaughter house offal may best be disposed of by burial in the contaminated area.

Advice as to the Drinking of Water in the Contaminated Area

If possible, no water should be drunk in the area. If canteens are to be taken in, troops must be drilled in the matter of drinking without contaminated the mouth of the canteen. Large amounts of water may have to be taken in - this greatly increases your responsibility.

The water in an area may be contaminated as a part of the general area contamination or may have become contaminated up-stream. What can be done about decontamination?

1. Physical

- a. Boiling. This is obviously useless or may be harmful. It is unlikely that all contaminants will be volatile. Boiling will then serve only to concentrate and increase the contamination.
- b. Storage. This time-honored and often successful method of water purification, though useful for short-lived isotopes, is impractical for field operations and of little benefit for long-lived isotopes.
- c. Filtration. Here we may be somewhat more hopeful especially hopeful since experimental work is being done and the value of filtration as can be applied in the field will be established.

- 2. Chemical
 In the sense of applying the usual water purification techniques (chlorine) this is obviously useless.
- J. Physico-chemical

 If we can combine precipitation and filtration, we may greatly reduce the load on filtration. Here again methods must be developed that are applicable to the field. Experimental work is being done by the Atomic Energy Commission and the Armed Forces to evaluate existing purification methods and develop new techniques or modify existing methods.
- 4. Biological
 Although activated sludge is usually thought of as being applicable to sewage and waste treatment, biological processes may well lend themselves to the problems of water decontamination.
 Such methods would not seem to be adapted easily to field requirements.

Prevention of Dissemination

Prevention of dissemination by personnel is often of great importance. The underlying principles are always the same and may be illustrated by a discussion of the evacuation of an area.

- 1. Decontamination center for area evacuation.
 - a. Clothing change and bathing facilities.
 - b. Laundry (decontamination) facilities.
 - c. Monitoring facilities.
 - d. Eating and surgical dressing only on "clean" side.
- 2. On entering contaminated zone.
 - a. Remove all clothing (or outer clothing).
 - b. Leave all smokes and eats behind.
 - c. Go to "dirty" side and put on work clothes (everalls, hat, gloves, and boots)
- 3. On leaving contaminated zone.
 - a. Remove hat and gloves
 - b. Wash face, neck, and hands thoroughly five times with soap and water.
 - c. Remove remaining clothing.
 - d. Soap and thoroughly wash entire body five times.
 - e. Go to monitoring room (between shower and clean side).
 - f. With permission of monitor go to clean side and put on original clothing.

Mortuary Considerations

Morticians and others having to do with the dead will be guided by the same principles and employ the same general precautions as will the evacuation parties and first aid groups. Irradiated bodies do not constitute a radiation hazard; contaminated bodies must be handled with the same precautions as apply to other contaminated objects.

Mortuary considerations may be discussed under three headings as to time and circumstances.

1. Air Burst

a. Any time after explosion

There is no radiation hazard to be anticipated since there will be no appreciable contamination and induced radioactivity will not be sufficiently great to endanger the mortician or his staff. This assumption must be checked by the Radiological Safety group and if verified, the bodies may be handled without regard to further radiation precautions.

2. Burst leaving appreciable contamination.

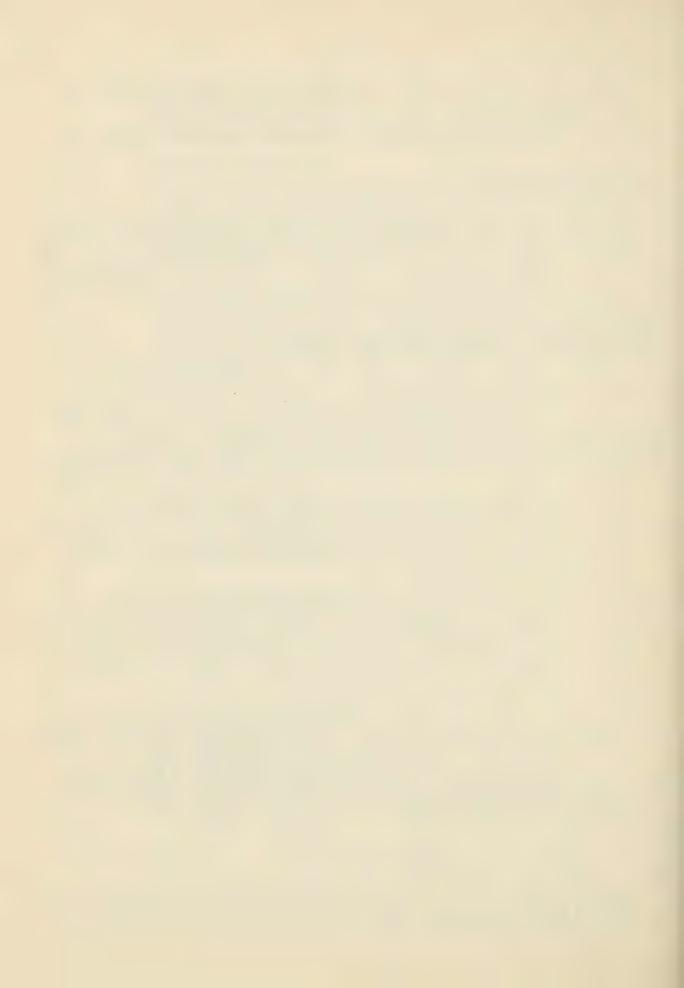
a. Immediate handling of bodies

For purposes of identification, burial on the site or removal for burial, the mortician and his staff must work under the continued advice of the Radiological Safety group. The first question is, of course, how long can the party stay in the contaminated area. The answer will be based upon the type and degree of contamination. Protective clothing will be worn. Ordinarily, where possible, this will be light weight disposable clothing, covering head, hands and body. If practical, bootees will be worn over shoes, but in field operations a change of shoes may be necessary. If the bodies are to be buried in the area without embalming, it will be necessary only to handle them in such a way as not to transfer contamination to the worker. For this, protective clothing and reasonable care will suffice.

If they are to be embalmed and moved out of the area, they should go through the decontamination procedure in much the same way as evacuees but the degree of decontamination need not be so thorough, i.e. contaminated clothing and readily removable surface body contamination should be removed. For ease of operation, rubber gloves may be used in place of cotton gloves for embalming procedures.

b. Later disinterment and shipment.

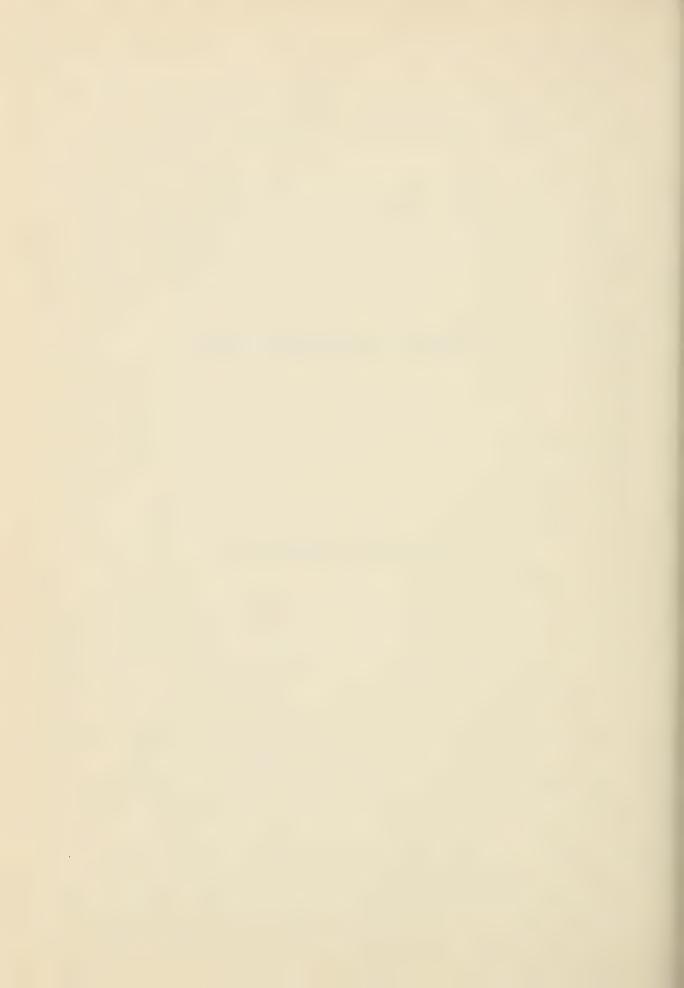
This will usually occur sufficiently long after the explosion so that the amount of radioactivity will be greatly reduced. Therefore there will be little question as to hazard to the mortician. He will be guided in this regard by Radiological Safety advisors. Since the bodies will be in sealed caskets, there will be no serious question of contaminating the areas to which they are sent.



TREATMENT OF ACUTE RADIATION ILLNESS

By

Major Albert J. Bauer, M.C.



TREATMENT OF ACUTE RADIATION ILLNESS

Major Albert J. Bauer, M.C.

At one time or another, almost every drug in the pharmacopoeia has been recommended for the treatment of acute radiation illness; as you might expect with such a multitude of cures, none of them produces astounding results. It is the purpose of this paper to present an outline of a course of practical therapy based on what we know today. As work continues, it is hoped that the discovery of a specific will render this effort obsolete, but until such a discovery is made, we must make every effort to be prepared to do the best we can with the tools available. Since the strain on our medical facilities will be great, it is just as important to shun uneffective procedure as to institute effective ones.

Most important in the handling of cases is the maintenance of water balance. These patients are nauseated, vomit and develop diarrhea. The water loss may be excessive and oral intake will surely be low. Once dehydration is allowed to develop, the problems of acid-base balance will complicate the treatment. Time and effort can be saved by the early use of intravenous saline and 5% glucose.

Almost as important as fluid balance is the maintenance of an adequate diet. These patients have undergone tissue destruction and the materials for repair must be provided. This becomes a difficult problem in a person whose gastro-intestinal tract has received a major insult. It is impossible to orally feed these patients to a point where the daily dietary requirement of 3,000 to 4,000 calories, including 150 to 200 grams of protein, can be met. Every dietary trick, including the use of lactose and predigested food, must be utilized. Oral intake will have to be supplemented by intravenous feedings. It is interesting to note that 1,000 cc of blood plasma, that is the plasma from 2,000 cc of whole blood, will furnish between 50 and 60 grams of protein. Plasma being a complete protein, this will just about meet the daily nitrogen requirement. One thousand cc of plasma represents about 250 calories so additional calories must be supplied through the use of glucose. The continued administration of plasma tends to decrease red ceil production and an occasional whole blood transfusion should be given when indicated. Every effort should be taken to aid the gastro-intestinal tract in its recovery by the use of emollient drugs and foods, and gastric sedatives.

The vitamin intake must be maintained. With the two following exceptions, no specific vitamin therapy has proven advantageous and the exceptions are themselves questionable. It has been claimed that Vitamin B6 will decrease the incidence of nausea in patients undergoing X-ray treatment. It appears that B6 is more effective in preventing nausea than in relieving the symptom once it has developed. It therefore appears

expedient to administer 25 Mg of Vitamin B6 daily to all patients who have received substantial radiation exposures. Work with Vitamin C indicates that it favorably effects the recovery of white cell production and its administration is also recommended. Of course the demand and the availability of these drugs will influence the decision as to its routine administration.

At present toluidine blue and protamine sulfate give promise of controlling the hemorrhagic tendency which develops in the second and third weeks of radiation illness. Doses up to 8 Mg/Kg have been given to hurans without producing toxic symptoms. 5 Mg/Kg have been reported to control hemorrhage and 3 Mg/Kg have been reported to continue control once hemorrhage has been stopped. Rutin has not proved too satisfactory and it should not be given along with toluidine blue.

Whole blood transfusions appear to have little effect on the hemorrhage but as the case progresses, the red and white counts fall; transfusions become necessary to furnish the means of oxygen transportation along
with white cell and antibodies to bolster the body's bacterial defenses.
The number and frequency of transfusions will depend on each individual's
response and the availability of whole blood. Unless the exposure has
been overwhelming, the bone marrow will regenerate if given time. The
rationale of whole blood transfusions, in fact of all recommended therapy,
is to provide time for this regeneration to take place.

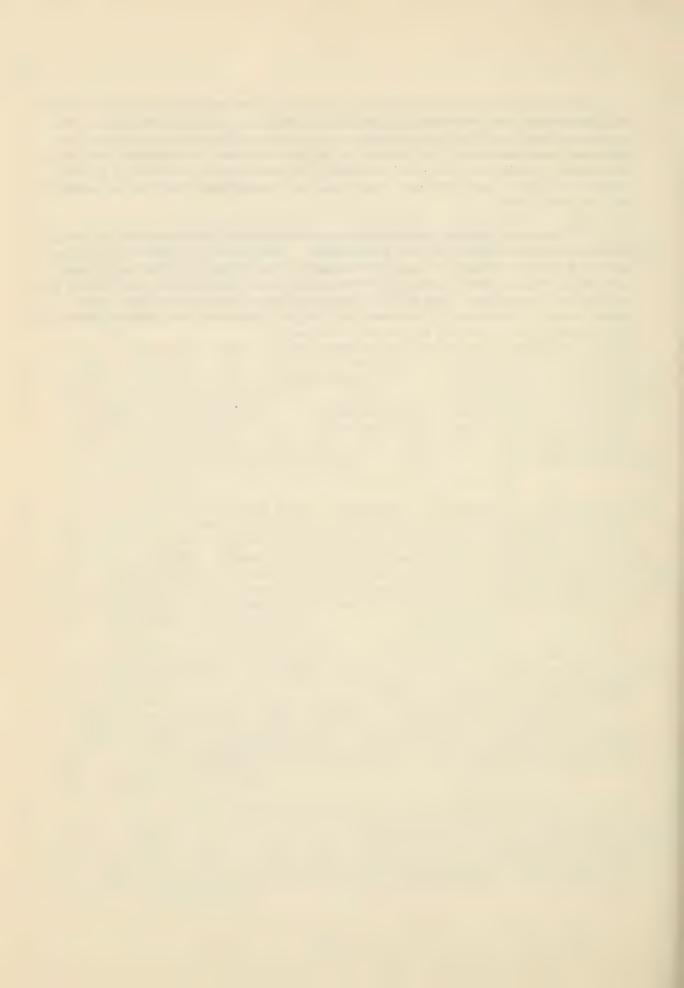
As the white count falls, infections will develop and spread. The free use of antibacterials is recommended along with transfusions as indicated. These patients greet all types of trauma with poor bacteriological defenses. Therefore all procedures where the skin is broken must be done under sterile conditions and the maximum use made of each traumatic procedure. In severe cases, it is probably wise to institute a continuous intravenous drip of normal saline and 5% glucose and use this channel for all parenteral administrations.

The epilation which may occur in the second or third week does not respond to treatment. It is mentioned here because of its adverse effect on patient morale. If the patient is warned to expect this development, assured that it has no bearing on the final outcome of his case, and appraised that the hair will return in a few months, a great deal of psychic trauma can be eliminated. It must never be forgotten that these patients will be apprehensive and anything that can be done to reassure or make them more comfortable will be helpful, including the free use of sedatives when indicated.

Many other measures are under study or have been recommended from time to time but at present none of them has proven of definite value. The use of adrenal cortical hormone or its substitutes should receive special consideration. There is some indication that its use offers protection to the liver - if it is available, it should be used on a series of cases to test its effectiveness.

It must be kept in mind that many of these patients will be suffering from burns and traumatic injuries as well as radiation illness. The necessary debridements and surgical procedures should be carried out as soon as possible after the radiation injury has been received as the poor response to infection and the hemorrhagic tendency which develop in the second and third week dictate that surgical procedures be kept at a minimum at that time.

The above suggestions are merely thoughts on therapeutic measures stimulated by a review of the literature. They are not presented as hard and fast rules. They are open to change at any time. It is hoped that hey will be of some value if an emergency develops and you are called upon to decide the proper allocation of medical supplies between numerous casualties. Undoubtedly the availability of supplies and medical personnel will govern the type and extent of treatment.



THERAPY AND HANDLING OF MECHANICAL AND THERMAL INJURY FROM THE ATOM BOMB

By

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THERAPY AND HANDLING OF MECHANICAL AND THERMAL INJURY

FROM THE ATOM BOMB

By

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The energy released by the explosion of an atom bomb is of an order of magnitude unsurpassed by anything known to man. In addition to large amounts of radioactive energy, great quantities of thermal and mechanical energy are released. It is these latter two categories of energy that produce the great physical damage, large number of casualties, and utter demoralization of the population subjected to the explosion. Photographs of the damage done by the atom bombs in Japan emphasize the magnitude of the damage from mechanical and thermal effects, and give mute evidence of the human demoralization and disorganization which takes place after such catastrophes.

Injuries to personnel from the atom bomb explosion have been divided into three categories: (1) Radiation injury, (2) Trauma, (3) and Burns (Table I) (4 and 8). Radiation injury is covered elsewhere in this manual. The arbitrary separation of the medical effects of the bomb makes the approach to the problems raised more simple, but it should be borne in mind that one individual may have all three types of injury, and, as has been pointed out by Parsons (10), can be killed "three times over". For purposes of clarity therefore, the remainder of this paper will be devoted to the traumatic and thermal effects of the bomb alone.

Trauma of the primary type, due to blast alone (Table I), is difficult to evaluate. Apparently the blast did not have the trip-hammer effect of other high explosives but was more like a sudden violent gust of hot air, which lasted over a relatively long period (2). Pulmonary and other visceral blast effects were not noted, nor was the incidence of perforated eardrums excessivley high (4).

The distribution and amount of secondary trauma was dependent on the distance from the ground center of the explosion. Within a radius of 2.4 km. there was complete collapse of the native wooden buildings. Within this zone, the incidence of mechanical injury was very high, dropping off gradually to less than 14 percent beyond 2.7 km. (2)

Table I

Typ	oe of Injury		Total Per Type Injury (4,8)	Totals (7)
I. Radiation A. Prim B. Seco	nary		over 30%	15%
B. Sec d d c 1. 2.	mary - Direct result of blast condary - Flying lebris, such as collapsing build Fractures Lacerations Contusions	glass,		
III.Burns A. Fla B. Sec	ash	95% 5%	65 - 85%	

The injuries consisted of fractures, lacerations and contusions. The low incidence of fractures (at least in the hospital given as the usual example - Table I) is probably because persons with major fractures were unable to seek treatment, or perished in the collapsed buildings. There is no evidence that these fractures were unusual in any respect. The contusions did not seem to be remarkable. The high incidence reported for these injuries is probably explained by the fact that they are relatively minor, and permitted the individual to seek treatment.

The lacerations were of interest in that they were largely due to flying glass fragments. These fragments were so small that clothing protected the individual in some instances. In other circumstances the fragments were of such size as to make removal difficult. Multiple lacerated wounds were very common.

The exact amount of morbidity and mortality attributable to the traumatic factor in the Japanese explosions will probably never be known, because immediately following the blasts, fire and disorganization prevented adequate and early rescue measures. It would seem reasonable, however, to suppose that both the morbidity and mortality from the traumatic factor could be greatly reduced by a properly organized and functioning rescue system, instituted early. Once the casualty is in the hands of medical personnel, treatment itself should present no unique

problem other than that of materiel. It might be important to treat these cases (particularly the lacerations) vigorously, and in a definitive manner, all possible effort being made to effect healing within the first two weeks, for thereafter the major effects of irradiation sickness begin to appear. If the casualty were close enough to the hypocenter to receive much ionizing irradiation, irradiation sickness resulting, his unhealed wounds would break down, infection of uncombatable degree would supervene, and death ensue from even a relatively minor injury.

The largest, and most important category (numerically) of atomic bomb injury is the burn. This group of injuries also can be divided into primary (due to the bomb, per se) and secondary (due to burning buildings, etc.) (Table I). Tsuzuki (12) estimated that about 90 percent of patients treated within the first few days were burned. LeRoy (8) estimated that less than five percent of the burns were caused by the fires in buildings and debris. There then remains a group consisting of ahout 85 percent of all casualties treated within the first week who were suffering from primary at a comb burns.

The energy which produced this high incidence of primary burns, had certain characteristics. The heat was intense, and largely radiant, with extremely high ultraviolet, visible, and infra-red components. The exposure was very brief - probably less than a second (Table II.).

Table II.

Components of Atomic Bomb Flash (2)

Temperature
Transmission
Spectrum

Est. at over 4000° C.
Largely by radiation.
High in Ultraviolet
High in Infra-Red.
High in visible light and
brilliancy.

Less than a second.

Duration

As with the traumatic factor, the thermal effects were closely related to the distance from the ground center of the explosion, the heaviest damage being within the 0.8 km. radius, the severity diminishing to practically nothing at 4 km. Because the thermal energy was largely radiant, effects were modified by shading of buildings, and the angle of incidence of energy. Clothing served as sufficient protection in some cases, light colored clothing being better than dark; however if the clothing were adherent to the skin by perspiration, burning occurred even through this protection.

The burns produced were of varied severity and distribution.
"Profile" burns were common, the parts directly exposed to the flash being burned most severely. Mild burns occurred, without vesication. These burns were usually sustained beyond 2 km. from the center and were intensely erythmatous within the few days immediately after exposure. However,

they gradually became pigmented finally attaining a "walnut stain" hue. This was most commonly seen on the face and therefore was called the "mask of Hiroshima". The pigmentation began to fade within a few months in some individuals, but in others has persisted for years (2).

More severe burns, corresponding to second degree moderate temperature burns, were frequent, but apparently did not carry the high mortality for large areas, seen in the latter type of burn. Vesication was present, and often appeared within a matter of minutes. More severe burns were sustained, and complete transfascial burns were found among the dead.

The course of these burns was, in some cases, benign, many healing with little or no treatment, despite some superimposed radiation sickness as well. However more often the healing was arrested or the burn turned to a serious one by the subsequent lack of treatment and resulting complications. The sequellae were remarkable for the large number of contractures and the high incidence of keloids (higher than noted in flame burns in Tokyo and other Japanese cities (3)). Both of these complications may well have been due to the lack of adequate treatment and the extremely poor nutritional state of these people. These keloids seem to become inactive with the passage of time.

The low incidence of flame burns has been explained on the basis of the time lag between the bomb burst, and the onset of fires. It is said that people escaped the fires if they were not severely injured. Those trapped in burning buildings perished, and no reliable figures are available on their number.

The care of a single traumatic or burned casualty, or a small group of casualties of such types as might result from an atomic bomb explosion, would present somewhat of a problem. Certain essential supplies and facilities would be required. These would include: (1) surgical dressings of all types, (2) morphine and sedatives, etc., (3) Antibiotics and similar agents, (4) whole blood and plasma, (5) hospitalization and/or adequate shelter of some type, and (6) medical and technical personnel. The volume of materiel and the number of personnel required to treat a single severely burned patient (approximately 40 percent of the body surface) in a modern hospital is approximately as follows: 42 tanks of Oxygen, 2.7 miles of gauze, 104 pints of fluids, 40 pints of blood, 36 pints of plasma, the attention of three nurses and two physicians and a quantity of drugs. Many such patients do not survive, despite such treatment.

The figures given for casualties at Hiroshima and Nagasaki are given in Table III. From these it can be calculated that the severely burned group alone, at Hiroshima probably exceeded 34,000! If it were necessary to treat all of these cases in a manner similar to the case mentioned above, the requirements in personnel and equipment would be staggering.

Table III

Atom Bomb Casualties (8)

	Hiroshima	Nagasaki
Population	300,000	200,000
Dead	80,000	40,000
Injured	40,000	25,000
Patients in need of immediate care	85,000	50,000

It seemed important, therefore, to reevaluate the modern therapy of burns, in terms of the burns produced by the atom bomb. This lesion has been called the flash burn. It is produced by an extremely high intensity wave of radiant heat, applied over a very brief period of time. Experimentally, various types of burns have been defined. It has been found that the more intense the heat source, the briefer the period of time required to produce a burn of a given severity. This is shown in some detail for the lower temperature zones by Henriques and Moritz (6) of Boston. However, the flash zone is being studied in detail in the laboratory.

Experimentally, many problems arise in the production of flash burns in the laboratory. The search for a suitable source is one of the most difficult. Certain criteria must be met to produce an ideal flash:

- 1. Transient duration on the order of 0.1 second.
- 2. Extremely high intensity, of a known degree.
- 3. A known or obtainable spectral distribution.
- 4. Safety and convenience of handling

Three general principles of flash production were tried: (1) the release of electrical energy from a bank of condensers to create a flash, (2) the creation of a constant high intensity source directed upon a target for known intervals by means of a shutter or trip mechanism, and (3) the use of substances that burn rapidly with an intense flame. The various sources tried, with appropriate comments, are listed in Table IV.

The flash produced by burning magnesium powder, has been used clinically to produce a burn, therefore this agent was chosen (5). The burns produced by the burning magnesium flash, have several interesting characteristics, most strikingly demonstrated in the histological picture. Most remarkable is the abrupt and diagrammatic demarcation between burned and normal skin. The normal, basophilic epidermal cells change on a straight line, to the acidophilic burned cells which have all characteristics of thermal injury. In the deeper skin, this demarcation is at

Rable IV

A summary of various sources tried (11)

Source	Duration of flash in seconds	Approximate temperature	Burn produce	ed Complication
FT14 Xenon flash tube	0.002	6300	None	Unable to focus energy
Exploding wire	0.00001	20000	None	Unable to focus energy too brief blast wave.
Thermite	Variable	3500	Not used	Spatter, low intensity handling difficult.
Gunpowder	To 1.0	3000	Failed	Low intensity
Magnesium	0.34	3500	Severe	Smoke
Carbon Arc	Constant	4000	Severe	Small area burn.

the burn border, in the crypts and hair follicles. It is present in the dermis but is less easily demonstrated. There is no gradual transition zone as in the moderate temperature burns. Another characteristic of the flash burn is the method of healing. The burned epidermis and dermis represents a coagulative "fixed" type of necrosis, with eschar formation and subsequent sequestration, rather than the organization seen in the non-coagulative necrotic tissue of the moderate temperature burn. With a flash-burn of average severity the epithelium grows out freely (and indeed beautifully) from normal borders and hair follicles, beneath the unorganized eschar so that healing is rapid. Yet if the area is large and the injury deep enough to destroy the epithelium in the crypts and hair follicles, then this characteristic demarcation will result in delayed repair from lack of epithelial islands (11).

Other factors about these experimental flash burns are their similarity to the ones noted clinically. For instance, severity diminishes as the distance from the source increases. Clothing and heavy creams seem to be adequate protection at reasonable distances from the source. Severity also decreases with the angle of incidence.

Despite the fact that more and more is being learned about the flash burn, little change in the accepted treatment of burns can be made as yet. It is possible that many of these burns will heal rapidly (if they are not too deep), provided adequate shelter and diet is provided the individual. The prevention of infection — by adequate dressings and antibiotics — will probably pay high dividends in the prevention of morbidity, sequellae, and uncalled-for fatalities. The entire problem is being studied from several approaches with some promise of a more practical and effective solution.

In conclusion certain facts should be emphasized.

- 1. Thermal and mechanical injuries account for the majority of the casualties from an atomic bomb.
- 2. From the experiences in Japan, 90 percent of all persons requiring medical attention in the first week will have burns and 60-85 percent of all patients will be burned.
- 3. The burns are of the "flash" type, produced by a high intensity, brief duration source. They are of all degrees of severity, and while some may heal speedily with little treatment, this is by no means a general condition.

 Sequellae and overall mortality probably will vary with the treatment.
- 4. Every effort should be made to evacuate the thermal and traumatic casualties early, and treat them vigorously, to reduce the incidence of complications from delay.

BIBLIOGRAPHY

- 1. Army Medical Museum, Photographic Laboratory, Washington, D. C.
- 2. Bliss, R. W. What You Should Know About The Atomic Bomb, A Message from the Surgeon General, Army Medical Department
- 3. Block, Melvin A., and Tsuzuki, Masao. Observations of Burn Scars Sustained by Atomic Bomb Survivors. A Preliminary Study. Amer. J. Surg. 75;417-434, March 1948
- 4. Brues, Austin M., Henshaw, Paul S., Block, Melvin A., Neel, James V., and Ullrich, Frederick W. General Report of the Atomic Bomb Casualty Commission, of National Research Council, Jan. 1947.
- 5. Fauley, G. B. and Ivy, A. C. Prevention of Flash Burns by a Protective Glove Film. U. S. Navy, M. Bull. 43:209, 1944.
- 6. Henriques, F. C. Studies of Thermal Injury. V. The Predictability and Significance of Thermally Induced Rate Processes Leading to Irreversible Epidermal Injury. Arch. Path. 43:489, 1947.
- 7. Lapp, R. E. "Must We Hide?" Addison & Wesley Press, Inc. Cambridge, Mass, 1949.
- 8. LeRoy, George V. The Medical Sequellae of the Atomic Bomb Explosion. J.A.M.A. 134:1143-1148, Aug. 2 1947.
- 9. Medical Radiography and Photography. 24:34-38. Aftermath A Pictorial Summary of the Medical and Other Effects of the Atomic Bombing of Japan. Eastman Kodak Co., 1948.
- 10. Parsons, R. P. Trauma Resulting from Atomic Explosions, Amer. J. Surg. 76:559, 1948.
- 11. Pearse, H. E., Payne, J. T. and Hogg, L. The Experimental Study of Flash Burns Ann. Surg. (In Press)
- 12. Tsuzuki, M. Report on Medical Studies of the Effects of the Atomic Bomb-General Report of the Atomic Bomb Casualty Commission. National Research Council. Page 67, Jan. 1947.

RADIOACTIVE DECONTAMINATION PROBLEMS

CDR. E. J. HOFFMAN, USN



CDR. E. J. Hoffman, USN

I have been asked to speak to you today on Radiological Decontamination Problems. This is a rather broad field and consists of several entirely different classes of problems to some of which the solutions are currently in a satisfactory state of development and others which are completely in an unknown stage. I will endeavor to cover such things in two phases depending upon how the contamination is received. The first of these is the ordinary contamination that may be received incident to the use of radioisotopes in the laboratory. The second of these is the considerations governing contamination received incident to use of nuclear weapons in wartime. The measures required to cope with contamination received by these two greatly different avenues are radically different.

I will consider the easy phase first. This is the problem of laboratory contamination. The best way to handle this type of contamination is to prevent it from occurring. This sounds like a trite statement but it is surprising that sufficient care is not always used to prevent unwanted radioactive materials from accumulating in places where they are not desired. The chief help in handling of isotopes is accurate and detailed planning of each operation that involves moving of the radioactive material. The commonest form of unwanted contamination is the contamination of glassware and counting equipment. The second form of unwanted contamination is that resulting from spills or unforeseen escape of materials. The third results from the disposal of materials upon completion of a test or experiment. In medical research the commonly used isotopes are in two general classes, those of relatively short half-life such as Phosphorous (P-32), Sodium (Na-24), Iodine (131), and longer half-lived materials extending to Carbon (14) with a half-life of approximately five thousand years. A laboratory is more apt to accumulate contamination when relatively long half-lived materials are used. The contamination received in the Laboratory will, of course, vary with the uses to which the radioactive isotopes are being put. If these materials are in some stage of process employed as a gas or compound with high vapor pressure, it may be expected that contamination will be more difficult to control and be somewhat more general. The methods of controlling contamination involve keeping track of the isotope from the time it is received until its ultimate disposal.

It is desirable to restrict the area in which the isotopes are used to the minimum consistent with satisfactory working conditions. All desks, floors, bulkheads and apparatus that are essential in this space should preferably be protected by a semi-permanent removable covering similar to "Tygon" plastic. Such material in the room which cannot be covered with the readily removable coating can be covered with paper or other temporary covering when danger of spills, or other containination may take place. When using the isotopes that have been noted, decontamination will consist of just plain scrubbing and washing with solutions that are known to be effective in rendering the tagged compound employed soluble and subsequently

disposing of the washing solutions. Obviously the minimum amount of washing solution will be desirable in order to reduce the bulk of the residue for disposal. When a space has been used for a considerable period of time with some of the longer half-life isotopes, it may become necessary to remove the entire temporary coating and recoat before resuming work. In carefully controlled experimental work the purpose for decontaminating will often be to reduce the background of counting equipment used, less frequently personnel hazards of the .lr variety will be encountered.

There are, of course, a great many isotopes that offer much different problems. They are not commonly used by the medical profession but they may be used in the future since they are becoming more available and may behave differently from a chemical or hazard standpoint. For all such small scale decontamination, radical changes in principle are not to be expected. If extensive work is planned with compounds which embody radioactive materials, it would be advisable to seek the chemical behavior of such compounds in the non-radioactive state to insure knowledge of the best washing compound to remove. It will be found that when the radioactive isotopes are added, they will behave in the same manner as the non-radioactive material upon which property depends their first usefulness.

We now come to an entirely different type of contamination and decontamination. This is the type which may result from the employment of nuclear weapons in warfare. As you no doubt know, there is not one but literally hundreds of isotopes produced in an explosion of an atomic bomb. Furthermore, when contamination is received, it is received by an area to which a great deal of preparation has not been feasible. At the time contamination is received it will be accompanied by panic and probably physical destruction. In other words, contamination is received under completely uncontrolled conditions and by generally unprepared areas. We will not be thinking of hazards of the .lr variety but of exposures that cause biological damage in a comparatively short time.

The considerations which govern the decontamination process will vary depending upon the method by which the radioactive materials are spread. The first objective will be to protect and reduce the exposure of personnel in the area subjected to contamination. The second will be to restore an area to unrestricted use, if practicable, but failing that to at least partial operability. We can do a little more than explore the considerations which are involved in the protection of personnel that are subjected to contamination. Because of the short half-life of bomb fission products, it seems today that the only feasible method of protecting personnel is by evacuation to a heavily shielded area or to an uncontaminated area as rapidly as possible. In order to illustrate how the effect of decay limits one's potential efforts we will cite a few figures: If one assumes that containination from a bomb is received at \$\frac{1}{2}\$ minutes, the subject will receive fifty percent of the potential exposure in one hour and a half. If contamination is received at \$\frac{1}{2}\$ minutes, fifty percent exposure will be received in 30 minutes.

In the practical solution the conditions are probably much worse than indicated due to the fact that considerable exposure of personnel is occasioned during the process of distributing contamination. These figures are cited to illustrate that adequate decontamination will not be any panacea for the deleterious effect of widely distributed radioactive materials.

I can probably lead you to the considerations which would indicate when decontamination might be required from atomic bomb detonation. With an air burst it is unlikely that severe contamination will be received in the immediate area affected by the burst of the bomb. It will, if it occurs at all, be due to freak atmospheric conditions which have not been experienced to date and result in contaminating an area some distance from the point of burst. The potential exposures that are probable in this instance are moderate. If, however, a bomb is detonated underwater or underground, contamination will be received in the vicinity of the burst over a considerable area but one which is distinctly limited, being of the order of several square miles.

The statement that one bomb could contaminate substantially the whole of New York City or San Francisco is ridiculous. The radioactive material will be spread uniformly over the area affected and will concentrate in those places which one would normally expect it to, as the result of its being suspended either in water or in dust. In the case of shore installations contamination resulting from an underwater burst will cause gutters, low spots, puddles and the like to be relatively "hotter" than the remainder of the terrain. The decontamination required in a shore establishment or a city area at the present time is seen as a project comparable to removing evidence of the smoky history of the city from many blocks of Pittsburgh. It will of necessity be first restricted to those areas which are vitally important. I believe that we can say that such areas as hospital buildings and access thereto, communication centers, transportation centers, and possible other installations will have enhanced importance in event of atomic attack on a city. The methods of removal of containination will vary with place or location which it is necessary to decontaminate. Obviously whatever method is employed on the outside of a building would not necessarily be suitable for an operating room, the methods employed on a concrete highway will not be satisfactory for clothing or food.

Specific methods cannot be cited for the many varieties of material which it may be necessary to use after an attack. However, it must be remembered that the radioactive materials deposited will behave exactly as any other compound, or dirt, that is deposited from a liquid or suspended in dust. It will be on the outside of tangible things. Materials which are subject to washing can be washed, the exact optimum washing compound is not yet known. At present the vegetable acids which form complexions with most of the fission products, which are in most cases soluble in water, of fer considerable promise. The problem is complicated by the necessity of removing such minute quantities of radioactive materials. The forces which bind one element to another in contact play a very important part in the decontaminating process. Another method of decontaminating is removal of the outer coatings of the object which is to be decontaminated if that

is easier. This latter method (sandblasting) has been used on ships and is a feasible method of decontamination to permit complete rehabilitation. However, it requires a considerable amount of equipment and time to accomplish. Very pourous materials such as unpainted wood, pourous concrete and pourous brick are not readily decontaminable by this method. One of the greatest misimpressions that is prevalent among wide segments of the populace is that some mysterious effect is had by the material itself as a result of contamination. This, as you all know, is quite in error. The phenomena of radioactive contamination is exactly the same as getting "dirty" except that very small amounts of "dirt" are required and the "dirt" is radioactive. One of the biggest factors in decontamination on the wide scale that has been indicated to be present, and which remains to be determined, is the statement of when is a building, a street, or an object, in fact, decontaminated sufficiently for use, or for use under limited conditions.

Another problem that will be encountered in decontamination is to secure the safe disposal of the removed material. This is one which is even further removed from adequate development as yet since it hinges on the practice of decontamination. In any area where provisions are made for drainage of storm water these will probably also serve as the avenue for disposal of liquid waste. Should there be extensive quantities of inert materials, mixed with contamination, such as might result from sandblasting, this will present a special problem. These materials may be piled up temporarily and covered with a cement coating to prevent scattering. Where important land areas such as railroad yards are contaminated, the addition of fixatives to the surfaces may be sufficient to permit use. Again it becomes impossible to cite specific disposal methods for the infinite variety of possible situations that may occur, each case that can be visualized, however, has an acceptable solution. Much hinges on precisely what is considered acceptable. In event of war it is almost certain that the concept of safe disposal will be liberalized.

In the course of our conversation we have considered, primarily, the case of radioactive contamination of shore establishments. In the Navy we are also concerned with the problem of radioactive contamination of ships. The principles and considerations which influence decontamination and disposal are the same. The problems involved are somewhat easier. Disposal into the ocean is usually convenient. By reason of its smaller area and high intrinsic value, it may be feasible to accomplish a considerable amount of pre-preparation to minimize the amount of radioactive material retained and facilitate its removal.

There are a great many more "problems" than answers at present. We believe, however, that in event it should come to pass that specific radioactive contamination situations arise, a specific solution will be available to accomplish the objectives of restoring an area or unit of material to usefulness. It will probably always be a hard task but distinctly not impossible or improbable.

COMMAND ASPECTS OF RADIOLOGICAL DEFENSE

By

Captain Frank I. Winant, Jr., U.S.N.



COMMAND ASPECTS OF RADIOLOGICAL DEFENSE

by

Captain Frank I. Winant, Jr., USN

Prudence dictates that we should be prepared for attack whenever a potential enemy is capable of delivering an attack. The United States delivered two atomic bombs within six years after the discovery of fission. Therefore, recognizing that others may attempt to match our performance, a readiness date of 1954 or 1955 for atomic attack would not appear early. Unless our defenses are superior to those of Hiroshima and Nagasaki, we can anticipate that an atomic bomb exploded over a major U. S. city will kill or wound on the order of 100,000 peopls. Of these, 40% will be killed and 40% will be seriously injured. The serious injuries will include burns, radiation sickness and mechanical injuries from collapse of buildings, flying glass and debris.

We rather expect that an enemy will try to burst his atomic bombs high in the air. When this is done, the instantaneous radiation will assist the blast and heat in taking a toll of lives. As at Hiroshima and Nagasaki, the lingering radiation from the bomb will be negligible. On the other hand, an explosion of the bomb at seriously reduced altitudes, whether by intent or accident, can increase the significance of lingering radiation.

Defensive measures against atomic explosions should lead to the saving of an indeterminate but considerable number of lives. Such defensive measures may be divided into four (4) broad categories:

(1) Material measures to prevent instantaneous personnel injury.

(2) Instructional measures to reduce instantaneous personnel injury.

(3) Preventive measures to stop the occurrence of personnel injury after the explosion.

(4) Curative measures to increase life expectancy of injured personnel.

Of these, the material measures seem most appealing. In theory, so much can be done. Wide application of such measures, however, appears improbable because of economic considerations. The concept of making every building proof against an atom bomb is perhaps more unsound than the Maginot Line theory of defense.

Where the importance of a particular objective demands, the proofing of structures against the atom bomb appears possible. The alternative is defense by dispersal. Insofar as we are bound to an economy characterized by large cities and large industrial units, we are highly vulnerable to atomic bomb attack. Under such circumstances, an atomic bombing like that at Hiroshima can kill more people than were killed by bombs throughout England in World War II.

Radiological Defense consists of protective measures to minimize personnel and material damage caused by radioactivity. Radiological Defense does not purport to make war safe. It cannot remove atomic bombings from the category of unspeakable disaster. But if it can reduce death and disorder, expedite recovery of a few thousand persons and permit removal of critical war materials, the defensive effort of training and equipping limited numbers of radiological defense personnel will pay for itself at any disaster scene.

Let us consider some ways in which radiological defense measures can pay off. We can instruct people with the object of reducing injuries provided they have a warning of the explosion. There may be no warning. But a fraction of a second will help. People can be taught to shield themselves. Thermal shielding is of greatest importance. A handkerchief over the face will help. A shirt, a blanket, a tree, anything between you and the bomb will reduce flash burns. At significant distances from the blast this shielding may effect the difference between hospitalization for thermal and radiation exposure as against medical treatment for radiation only.

Shielding against instantaneous gamma radiation is of comparable importance but it is harder to effect. Here again, anything constitutes a shield, but heavier shielding is necessary to give significant protection. Three inches of concrete, although inadequate at close range, might provide a major protective factor at greater distances. In many situations, substantial buildings can provide a degree of radiation shielding. There is, however, the need for an evaluation of the protection provided by various types of buildings to be found in a typical target area versus the hazards of collapse.

We can, with some hope of benefit, teach fundamentals of self help; avoidance of fire, radioactive areas and overcrowding.

The next defensive category consists of measures to prevent occurrence of personnel injury after the explosion of the atomic bomb. This field is of major significance to the military radiological defense personnel. It involves rescue of personnel as well as control of persons who must work in hazardous areas. The combating of fire will be of major significance in rescue operations. Many people who could have been rescued will burn to their deaths. Radiological defense operations should assist the general rescue efforts, which will include not only personnel recovery and fire fighting, but control of panic, logistics, communications and many other passive defense measures. Radiological defense must not impede the rescue of endangered personnel. It must not delay operations nor permit over-emphasis of the less significant hazards.

We must consider the controversial matter of lingering radiation such as that found on the Bikini ships. Regardless of indications in the press, the military have not underrated this hazard. Lingering radiation is one of the most optimistic features of the atomic bomb from the defensive point of view. It is the one thing about which we will really have time to do something. It offers a promise of successful countermeasures. Therefore, we have played it up in our service educational programs and in our service research programs. This year we are spending millions of dollars in the

National Military research and development programs to combat lingering radioactivity as against only thousands to combat thermal effects. This is going on in spite of our firm belief that thousands will suffer from thermal effects for every one who suffers from this so-called "lingering radiation". Since we can see the way clear to spend these millions intelligently and profitably, we will not cut back on such effort.

In a catastrophe so vast as that resulting from an atomic bomb, any preparatory effort which can reduce loss of life is justifiable. It is also worthy of a proper evaluation. Considering that lingering radioactivity will be virtually non-existent in the case of the normal airburst, such an evaluation places it low on the scale of hazards which will confront us. And if we engender in our radiological defense personnel and in our military commanders an unreasoning fear of lingering radioactivity, we shall probably take an unnecessary toll in American lives.

Curative measures will be concerned largely with mass treatment. Therefore, the logistic phases are very important. Provisions must be made for large stocks of blood and for dressings. Hospital space and medical personnel will be at a premium. The sorting of casualties to place the lesser injuries at first—aid dressing stations and away from the hospitals will be necessary. The problems raised here are different from the problems of conventional warfare only in point of the magnitude of effort and preparation.

The problems of radiological defense are of common concern throughout the military services. One important phase of our radiological defense training program is to provide the military commander with assistance in solving the unconventional aspects of these problems. The problems of radiological defense may be sub-divided into three (3) categories which I shall call:

- (1) Psychological aspects
- (2) Medical aspects(3) Technical aspects

The psychological aspects will prove hardest to deal with. For the Most part they deal with unreasonable fear.

Reasonable fear can be a useful thing in our lives. It can cause us to dodge an on-rushing automobile or to get inside of a tank or battleship or behind a machine gun. But the hazards of lingering radioactivity are the food of unreasoning fear. Such hazards are non-sensory. They cannot be seen nor tasted. They cannot be felt nor smelled. They can be internal or external, or both. They can be quick acting or long delayed. Lingering radioactivity is not mythical; it can range from insignificance in the case of a high airburst to considerable significance in the case of ground or waterbursts. It could have preponderant importance in the event of disaster in our own atomic installations or in event of an enemy's resort to some form of radioactive warfare. These versatile qualities of lingering radiation make it a powerful psychological tool. Whether or not we can use such propaganda features against an enemy, we can certainly let them work to our own disadvantage.

If psychological weapons are to be forged against us, let an enemy do it. Let's not penalize ourselves. The general thinking in military circles at the present time is that atomic bombs will be used to produce airbursts. So long as we feel that an enemy will not find it desirable to exploit the radiological features of the weapon, at a sacrifice in other destructive effects, we should not exploit these features for him and add unnecessary complexities to the panic which will probably follow an atomic bombing. We should not enhance the value of an enemy's weapons by making them psychologically more potent. Radiological hazards should be assumed non-existent in an atomic bombed area until they are proven to exist. This would mean that the firemen, police, stretcher-bearers and medical personnel would have immediate and free access to stricken zones. Radiological monitoring must be conducted promptly to confirm the assumption. This places upon the shoulders of the radiological defense organization the problem of being ready and having personnel at any atomic bombing scene promptly in event of a true radiological disaster.

If the airbursts of Hiroshima and Nagasaki and Test ABLE have established a prima facie evidence of small lingering radioactivity from a high airburst, certainly Test BAKER has provided room for doubt in other instances. It seems reasonable to assume that an enemy will create some radioactive areas in the United States, even if only from a malfunctioning of bomb fuses. These areas will constitute major problems in radiological defense. We can and will work in such radioactive areas. Our atomic tests have proven this. But we must work intelligently.

The military commander will have medical advisors to assist him. But how much physical injury will he accept within his own command. Where and how will he "draw the line"? It is my opinion that the wartime military commander in a radioactive area will establish a limitation for personnel exposure which I shall call the "Wartime Military Tolerance" (WMT). This is an arbitrary guide which will limit the time that personnel may be employed in radiological areas. It can be established as an arbitrary percentage of the median sickness dosage as indicated in the following equation:

WMT - K x MSD

MSD means "Median Sickness Dose". It is the cumulative dosage whi... will cause half of all persons exposed to it to become radiological patients. Such persons will have received some physical injury. There will be blood changes involved and we can say that the men are radiologically ill. MSD has not been defined with finality. It will vary with the rate of exposure. It may run as low as 100 roentgens for very rapid exposures and higher than 200 roentgens for low rates of exposure.

The determination of what constitutes median sickness is a matter of medical research and is not a problem of military command. In terms of conventional warfare, MSD might correspond to the probability that a bullet injury would necessitate hospitalization - obviously not a command but a medical problem.

The equation suggests that WMT, the largest amount of radiation to which a military commander can afford to expose his men, is a certain percentage of the median sickness dosage. We want WMT to constitute a suitable limitation which the commander can prescribe throughout his organization. Its value will depend on the proper choice of the control factor, K.

Let's examine the significance of this control factor. We will find that it must be appreciably less than unity, and appreciably greater than zero and that the exact positioning between its upper and lower limitations will be controversial. The upper limitation will be a medical control. If we let K equal unity and allow personnel to work in radiological areas until they have accumulated up to 200 roentgens then we shall require the hospitalization of fifty percent (50%) of our rescue personnel at a time when all hospitals in the area are already hopelessly overloaded with atomic casualties. On the other hand, we shall find that the prompt medical injuries will decrease as the value of K is decreased below unity. For example, if K were established at 50%, then we might expect less than 10% of our rescue personnel to become radiologically ill. Under wartime circumstances the losses would not be deemed serious. Injuries resulting from a K of less than 50% would probably be more on the psychological than the physiological side.

There is another consideration in establishing the upper limitation of K which I will call a "margin for error". When a wartime military tolerance is established it is meant to be an actual working tolerance to which the local commanders can subject their troops with assurance. Therefore if WMT lies right on the borderline of physical injury, we shall find that those persons who unwittingly exceed the WMT will be endangered. This is not desirable. It is almost impossible to insure that some personnel will not exceed any established limit, or putting it another way, you can assume that 5% to 10% of employed personnel will exceed existing limitations and that a very few persons will significantly exceed them. It will be of great advantage to us if we can assure all personnel that the standards which we establish are sufficiently safe so they are positively guaranteed against radiological injury. On this basis I would say that the value of K ought not to exceed 40%.

In considering the lower limitations of K, we are concerned with technical problems and must make provisions for operating efficiency of our personnel. How safely can we work in a radiological zone without falling below a scale of diminishing returns so that the value of the work accomplished is not commensurate with the effort expended? The absorption of radiation is never desirable and should never be permitted unless necessary. But when we get down to a value of K on the order of 10%, we begin penalizing ourselves and encumbering the personnel to a point where they cannot work efficiently in areas that are appreciably radioactive. During Operations CROSSROADS and SANDSTONE the value of K was on the order of 2%. Work in radioactive zones was carefully planned to permit the personnel to quickly enter these zones and secure information or equipment of scientific value. Even with this careful planning the work was considerably hampered by the high degree of personnel protection which we maintined. some instances personnel arriving in radioactive areas were scarcely able to orient themselves to a job before they found it necessary to withdraw. Such operations led to fast Jeep rides over rough terrain where the reading of

radiological instruments became inaccurate and sometimes defeated the prescribed precautionary measures. It would be practical in wartime to work in radiological areas to a point well beyond the SANDSTONE limitations without detrimental effects upon personnel. On occasion the desire for extreme caution leads to more serious hazards of other natures. For example, in the ammunition removal operations on the Bikini vessels after Operation CROSSROADS, the extreme precautions for personnel involving the wearing of rescue breathing apparatus to protect against possible, but actually insignificant, concentrations of radioactive material in the air led to the amplification of explosive and other types of physical hazards. The poor vision afforded by the rescue breathing apparatus was a contributing source of difficulty. One man received a glancing blow on the forehead from a five inch powder charge which fell the length of an ammunition trunk on the NEVADA. The actual injuries received in these operations were negligible but the hazards were potentially great.

There can be a very real danger from increasing our protective requirements too greatly. If we set K at 10% the time will come when a local commander will be more impressed with the inefficiency of his command than with the need for protection against radiation. He will become aware of the fact that radiation within his command is harmless and at the same time he is failing to get a job done because of extreme precautionary measures against radiation. is liable to kick over the traces and assume that radiation hazards are overrated. He may issue orders that the job be accomplished regardless of the hazards involved. This is about the worst thing that can happen because the hazards are there no matter how intangible they may appear and they will inevitably take a toll if suitable precautions are disregarded. For this reason the working limitations should be reasonable to a point where the local commander realizes that he must not exceed WMT but that the established value of WMT will allow him to work with the greatest possible freedom. With this in mind it would appear that the value of K could profitably be set at 20% and that any value below this would unnecessarily restrict the efficiency of the organization and might possibly hamper the protective measures themselves.

The next problem becomes that of establishing a reasonable value of K somewhere between the upper limitation of perhaps 40% and the lower limitation of 20%. The major influence in determining the proper establishment of this value would appear to be psychological. No matter how hard we may try to calmly evaluate radiation as a hazard and place it in its proper scale with other forms of military hazards it has psychological aspects which simply do not fit our normal modes of approach. Let me illustrate this by discussing what I call, for lack of a better term, the "furnace factor".

Suppose, for example, that you approach a group of men with the idea of obtaining a hundred volunteers to crawl through an area where they will be exposed to well controlled machine-gun fire as a training confirmation. You give them assurance that they will be carefully watached and that the fire will be terminated if an injury to anyone is noted. You would not expect too much difficulty in getting volunteers for this mission during wartime training. "Hope springs eternal in the human breast". There is a possibility that one man may get hurt, perhaps killed, but each man with a faith in his

own destiny knows that it will be somebody else, and that he will be safe. Now, to recognize the psychological pitfall introduced by a non-sensory danger, let's change the problem to one in which the fate of every man is pegged to that of his comrade. If a group of men were standing in a blast furnace when the heat accidentally went on, you would expect reasonable uniformity of injury to each man in the group, regardless of whether the flames were devastating or quickly quenched. If a group were standing in the beam of a giant x-ray machine one would expect no preferential protection. It is hard to find an anology in conventional warfare, but perhaps we could subject the group under machine-gun fire to a more uniform hazard. Let's change the problem by turning on a battery of flame throwers while the men are in the control zone. Assure them that the heat will be turned off as soon as any injury to personnel is observed. Draw your own conclusions as to how many volunteers you will get for a task like this. In the first example each man has 99 chances out of a hundred of survival whereas in the second instance every man should meet a fate as bad as that of anyone in the group. Whether he gets burned to death or just gets his hair singed, each man is sure that he will get treated just as badly as his companion. This is about what might be expected by personnel working in a lethal radioactive zone and the expectation may prove unpopular. Gamma rays are not respectors of persons. Whether they subject everyone to a withering dose or to an insignificant exposure, they hit everyone in the target area with almost identical effect. To understand the psychological factors which this creates, you must consider the ideas, trivial or otherwise, that run through the minds of your soldiers. They will think about this sort of thing when they are confronted with hazards which they can neither see nor taste nor feel nor smell but which they, nevertheless, know are having physical effect upon them. Such hazards prey mostly upon the mind. The men must have a powerful faith in the commanding officer to work continuously and calmly in the presence of unobservable but certain hazards.

If you hope to get the most out of the men you will recognize the significance of this intangible but highly important emotional factor and prepare them psychologically for the work in which they are to be employed. One of your strongest talking points in such a psychological campaign will be the assurance that you have held the K factor down to the lowest reasonable value; in other words, that you have virtually eliminated the so-called "furnace factor".

Now let me emphasize once more that we would not expect highly radioactive zones in the average atomic bomb explosion. Radiological defense concerrs itself with readiness for the instances in which such residual radioactivity is found. If radiological defense measures are to be invoked when
they are needed then we must prepare for them now by training and equipping
personnel to comply with their missions when required. We must expect atomic
bombs in future wars. We must expect injury and it is proper to assume that
we will encounter residual radioactivity in some circumstances. Such radioactive zones will not necessarily contain rates of radiation which would
approach lethality under normal working conditions. But we can expect significant dosages.

The areas bombed may be our most important installations - atomic plants, ordnance plants, big industries, the things which we must restore to operation if we are going to carry on the war. If we approach the problem with the assumption that such an area is radioactive and if we put a big fence around it and stay out - we are licked! We can, and must, work in radioactive zones. But we must work in them under controlled conditions. We can't go to the commander and say, "Now, there are no hazards in here at all. You are free to work". What we can say is, "We would like you to attempt work, but it will be dangerous. You must be prepared to work for limited periods only. There will be over-exposures. For this reason you must have replacements at hand. Exposure records of personnel must be maintained. Personnel must receive qualifying physical examinations, since a limited number of people can thus be separated as undesirable radiological risks for such work".

The technical aspects of Radiological Defense constitute a field in which much has been done to assist the commander. The Radiological Defense Officers will be important assistants to him. More than one thousand have already been trained, and we are training about that number yearly in joint courses conducted by the Army, Navy and Air Force at Edgewood, Treasure Island, and Keesler Air Force Base. These are the personnel who will assist organizationally. They understand the calibration and use of detection instruments and the nature and evaluation of radiological hazards.

In this discussion, my references to radiation have implied gamma radiation, the long range killer, which I consider the most significant type of radiation. There are others. For example, alpha and beta emissions will have great significance where lingering toxic effects are to be feared. Underwater bursts or surface bursts may contaminate your zones with a multiplicity of fission products in the form of radioisotopes. Rates of decay will eliminate certain fission products as significant hazards after a period of time and the readings which are obtained from certain types of detection instruments may become negligible. Such fission products may be superseded by others as principal hazards. Under circumstances where sabotage is involved, the most serious hazards may be hardest to detect. Such complexities point up the need for special personnel and equipment and give rise to serious problems of personnel and material decontamination.

Protective equipment for the workers consisting of masks and disposable clothing may be indicated. Careful monitoring of radioactive areas and supervision of workers will be necessary to prevent operations of personnel in "hot spots" of radioactivity. Field laboratories and special technicians for the analysis of radioactive materials and to determine the freedom from toxicity of air, water and food may be necessary. Training of specialized personnel has commenced and development is under way on all necessary types of instrumentation and equipment. It is hoped that the current service research programs may lead to some simplification in the complex material requirements of Radiological Defense.

Radiological Defense is a responsibility of command. The establishment of a wartime military tolerance will provide a planning guide for the military commander. It will enable him to complete requirements for timely replacement of personnel. It will be a guide in protecting personnel against external radiological hazards but will not be an absolute limitation placed upon the commander. Under conditions where personnel must travel through or work in atomic areas with the only alternative being destruction from other causes, any established tolerances would serve no purpose.

Realizing that no simple guides will prove unfailing and that complete reliance upon specially trained advisors is not always expedient, the current program for radiological defense training is aimed at service-wide indoctrination.

Over and above our training programs, there will be many operational problems for which there is no simple scientific or text book approach. Our training program admittedly needs stiffening along these lines. There is very little realistic experience upon which to base standard operational procedures. We have had atomic bomb bursts under conditions of war in Japanese cities but the residual radioactive conditions were lacking. We have had a series of atomic bomb tests but these were not associated with the disaster conditions to be expected in wartime. We can say one very definite thing about radiological hazards. We may not have them associated with every atomic bomb burst. We may not, and we probably won't. But when we do have them, the radiation hazards will invariably be associated with cataclysmic destruction resulting from the atomic bombing in the form of vast numbers of injured personnel, fires broken water mains, gas lines and electric wires, disrupted communications and the probable failure of logistic support and panic. Our operational development must be guided by the fact that our radiological defenders in accomplishing their primary mission, must work in the presence of these other complex problems.

The normal employment for radiological defense personnel will be in areas of sub-lethal contamination. Our efforts must be to determine what we can do, rather than what we cannot do in these areas. We can and will work in them when there is cause. We will not sacrifice vital industry and war plants simply because they are contaminated with a radiation level of 10 or 20 roent-gens per day. Under such conditions a well trained staff group will be indispensable in prescribing the working conditions, techniques, lengths of exposure, protective devices, decontamination procedures and in providing adequate supervision.

We should not disregard the possibility that many of our personnel trained for radiological defense may be called into disaster areas even in event of high altitude atomic bursts. There may be no need and no reason for this other than the fact that these people have had a special training course.

We must not leave our problems of operational development unsolved awaiting a hurried solution under conditions of actual warfare. Future atomic tests should be very useful for developing our standard operational procedures and organizations and military personnel should be employed in radiological defense work in these tests to increase our service experience. These tests are few and far between and are sometimes limited to specialized objectives. Since they fall short of the disaster conditions toward which our planning must be pointed, it seems vital that there be operational development within the services. We have a great deal to do in properly evaluating the air reconnaisance of radiological areas, in determining the value of helicopters for radiological survey, in perfecting remote and projectable telemetering instruments and techniques and in completing time studies and work planning and on-the-spot orientation methods for such conditions. We have a great deal more planning to do in the matter of provision of adequate and timely personnel replacements in radiologically hazardous areas.

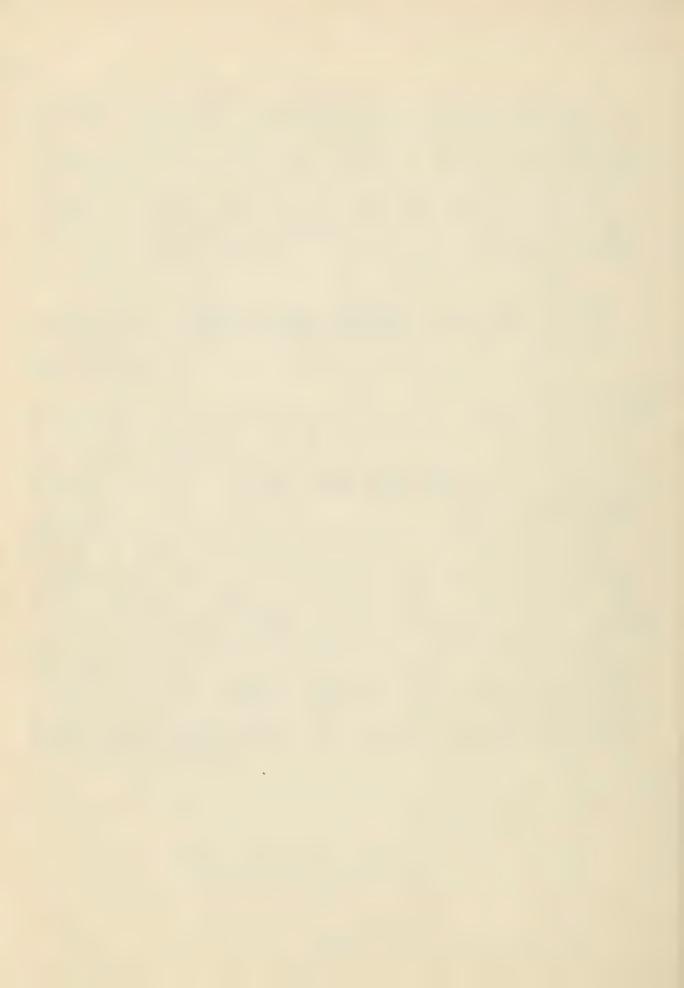
Operational development work will provide a continuous testing of textbook training and prevent stagnation of training doctrine. Without it our training in theoretical aspects can advance only to the limit of the most recent physics text and in its practical aspects to the limits of the last information which has enamated from atomic tests.

No discussion of this nature could be complete without some reference to Civil Defense. Since most of us have families, we are naturally interested in this problem. The armed services are responsible for effecting their primary military missions in wartime and will, in general, be unable to effect civil defense. Recognizing this condition, it is proper that the military should keep out of civil defense as much as possible. This will confront the Civil Defense Organization with the responsibility of growing up to meet its own problems. It would be sheer folly, however, to overlook the fact that civil defense will have a great influence on our capabilities to wage war. The next war may very well be won or lost on the home front. Recognizing this, we are trying to do what we can in support of civil defense without complicating it. Our research programs are pointed toward developing equipment which will be as useful to the civil defenders as to the military. The field of radiological defense, from its inception, has been a universal field with universal language, equipment, techniques and training. It is a military goal to increase our readiness in equipment and trained personnel so near to the service requirements that if called upon in emergency we can release radiological defense personnel to any point necessary. To this end we have initiated a truly joint training program with the Army, Navy, and Air Force turning out of their own schools, joint student groups who have been trained in joint curricula under joint staffs so that in emergency they can be banded together quickly and work together with intelligence and precision as they did in Operation SANDSTONE.

RADIOACTIVE ISOTOPES IN CLINICAL MEDICINE

By

Captain Edgar Leifer, M. C.



RADIOACTIVE ISOTOPES IN CLINICAL MEDICINE

Captain Edgar Leifer, M.C.

The purpose of this lecture is to present a resume of the clinical uses of radioactive isotopes. The major portion of the discussion will be confined to the diagnostic and therapeutic uses of the artificial isotopes but several experiments will also be mentioned to illustrate the potentialities of further investigations.

The production of artificial radioactivity by the use of a radium-beryllium source for neutrons, through the use of the cyclotron or through the uranium pile, has made possible a great deal of work on the use of radioactive isotopes in human physiology and in the treatment of malignant diseases. Several years ago it might have been possible in a talk such as this to present a fairly complete review of the uses of isotopes in medical research. Studies have progressed so rapidly that this can no longer be done. Of necessity, therefore, the discussion of each of the isotopes will be brief.

The first to be considered is radioactive sodium (Na24). Following its discovery in 1934 it soon became apparent that this isotope of sodium possesses many characteristics which make it particularly suitable for physiological studies. It has a short half-life (14.8 hours), is evenly distributed throughout the extracellular fluid, is a non-foreign and non-toxic substance. The radioactive atoms disintegrate by the ejection of a beta ray and the emission of powerful gamma rays which makes it possible to use Na²⁴ in in vivo experiments as well as in vitro. The quantities required in in vivo experiments produce an overall radiation of about 0.5 roentgen equivalent physical (rep), about as much as the chest receives in a routine chest x-ray. This isotope has been used in studies of electrolyte balance, extracellular sodium space, the mechanism of sodium shift in shock, and the transport of sodium through the skin, mucous membranes, the placenta and across the pulmonary epithelium in nebulized solutions. It has been used in the study of peripheral vascular disease and has been especially helpful in the determination of levels of good circulation in cases where amputation is necessary. It has recently been reported to be useful as a diagnostic aid in cardiac circulation.

Blumgart and Weiss in 1927 were the first to utilize radioactive substances in the study of the velocity of blood flow. They injected radium B into the antecubital vein of the upper extremity and studied the rate at which it would arrive in other extremities. Although it decayed with a half-life of 26 minutes, Radium D, an isotope of lead, was formed with a half-life of twenty-two years. This is deposited in bone and produces a prolonged radiation effect. Sodium²⁴ as has been pointed out, has none of these objections.

There are two methods for studying circulation in the extremities using Na²⁴.

- 1. Intravenous injection and study of the accumulation of Na²⁴ in the tissues.
 - 2. Rate of removal of Na²⁴ following intramuscular injection.

Following an intravenous injection of Na24 in the form of sodium chloride the time required for the Na24 to flow thru the blood vessels from the injection site to the site under investigation is determined with a Geiger-Muller tube placed over the skin. Thus the circulation time from the antecubital vein to foot has been found to be about 30 sec. The circulation time itself is not significant as a measure of adequacy of blood flow as it has been shown to have such a large variation in normal subjects. However, the rate of uptake of radioactivity and the equilibrium point reached are to some degree a measure of the volume of blood to an extremity if accurate standardization of the amount of injected radioactive sodium is made. In cases of extremely poor peripheral circulation if one determines the tissue radioactivity at different levels along an extremity, one can arrive at a line of demarcation between adequate and inadequate circulation which will give an amputation level. This method has provided useful information for the clinical evaluation of symptoms, circulatory insufficiency and the results of various forms of therapy in peripheral vascular disease (arteriosclerosis, Buerger's Disease, Raynaud's Disease) largely in the hands of Quimby and her co-workers.

The second method of circulation study using radioactive sodium is that of the injection of Na²⁴ into the muscle, e.g. gastrochemius muscle - the application of a Geiger counter directly over the injection site and study of the disappearance rate of radioactivity. This is most suitable for the study of drugs and the medical and surgical techniques for circulatory improvement.

Similar investigations by Tobias and co-workers have shown that in general there is a decreased circulation in patients suffering from rheumatoid arthritis which fits the clinical experience that many of these patients have cold extremities.

At this point it might be proper to mention that although the therapy in rheumatoid arthritis is largely empirical, many clinics have obtained encouraging results using gold. To study its action, radioactive gold salts were used to determine the distribution of gold in tissue samples. In one series of experiments, the labeled gold was injected I.V. into normal rabbits and into rabbits suffering from a chemically induced arthritis. Among the findings are the relatively high uptake of gold by the liver, kidney, and bone marrow (sites of toxic reactions) and likewise a high uptake in the involved synovial tissue. This is confirmed in rheumatoid arthritis patients but is not the complete story as gold is taken up by all areas of inflammation. This, too, fits with the clinical impression that patients who have evidence of active inflammation of joints are benefited most by gold therapy.

Since sodium is an extremely important cation component of tissue fluids, measurements of the dilution of tagged sodium atoms following their administration (allowing sufficient time for uniform mixing) are significant in determining the sodium space. Assuming a uniform distribution of sodium in the extracellular fluid compartment, the amount of radioactivity remaining in the body (amount injected minus the amount excreted) divided by the amount per unit volume of plasma (measured) gives the volume of fluid in which the sodium is dissolved, the so-called sodium space. The latter value usually runs about 5% greater than the extracellular fluid volume due to the deposition of sodium in the bone.

By determining the radioactivity in the urine, feces and blood plasma as a function of time, one can measure the sodium turnover of the body.

The problems of circulation would be incomplete without mention of the application of isotopes to problems of blood flow thru the heart in health and disease.

If one injects Na²⁴ into a vein and places a G. M. counter connected to a direct writing recorder over the precordium, one would expect to obtain an M shaped pattern - the first peak of the M as blood comes into the right heart and the second peak as blood comes into the left heart. This pattern has been called a radiocardiogram by Prinzmetal and his co-workers. The distance between the peaks represents the pulmonary circulation time. In congenital heart defects and in heart failure, one would expect variations from the normal M shaped pattern. Present methods for diagnosis of congenital heart disease consist of careful history and physical examination, X-ray and fluoroscopy of the heart, electrocardiogram and cardiac catheterization. Radiocardiography may become an additional important diagnostic tool, and has already been found useful in the diagnosis of patent ductus arteriosus.

The absorption of ions, both positive and negative, from the gastro-intestinal tract as well as from the lungs, the skin, the vagina and other locations in the body has attracted considerable attention both from the standpoint of pure physiology and from the practical aspect. These investigations find application in almost every specialty of medicine, e.g. otolaryngologists have been interested in the passage of nebulized solutions of Sodium²⁴ to determine the efficacy of aerosols; ophthalmologists have been interested in the passage of Sodium²⁴ across the ciliary body of the eye.

Another isotope which has attracted considerable attention is radioactive iodine. Although there are several radioactive isotopes of iodine,
this discussion will be limited to I¹³¹ which emits both beta and gamma rays.
It has been known since the beginning of the century that radioactive materials
have destructive powers as far as tissues are concerned and can be used to
treat tumors providing the tumor is radiosensitive. A most significant problem
is the localization of the radiation in the tissue one desires to treat. Using external radiation, one attempts to do this by using lead shields and cross
firing. This protects the region around the irradiated area to a great extent
but the skin over the tumor region may receive an excessively large dose.
Using radioactive isotopes, one can take advantage of any of the following

- (a) Physiological Concentrating Ability to be illustrated by iodine.
- (b) Use of Colloids to carry radioactive element to a desired location in the reticulo-endothelial system, e.g. following the intravenous injection of radioactive gold or chromic phosphate (P³²) in the form of colloids, one can produce a marked selective irradiation of the liver and spleen.
- (c) Local Implantation of radioactive elements, e.g. radium needles or Cobalt 60 in the form of wire for interstitial use.

Radioactive iodine is important in therapy because of the marked pyshiological concentrating ability of the thyroid gland. Of a total of 25 mg. of iodine found in the human organism 15 mg. is in the thyroid gland. Since the normal thyroid gland weighs about 30 gm. and the total body about 60 Kg. the concentrating ability of the thyroid gland is about 2000 - 3000 times. Thus in cases of treatment which we will discuss, it can be readily seen that the thyroid gland will receive a large majority of the radiation of any amount of I¹³¹ fed to the normal person.

In the thyroid gland one finds that the inorganic iodine is converted to monoiodotyrosine (as has been shown recently with I¹³¹), then diiodotyrosine which in turn is converted to thyroxine which combines with a protein to form thyroglobulin the active hormone of the thyroid gland.

Before undertaking any thyroid studies it was necessary to determine at what level the thyroid gland itself would begin to show biological effects of radiation.

Skanse investigated the effects of radioactive iodine on the thyroid of growing chicks and finds beginning effects for about 1700 reps (roentgen equivalent physicals). Similar experiences in man where one attempted to treat thyrotoxicosis show that the thyroid gland appears to be effected by about 2000 - 3000 reps.

In a study of thyroid physiology, one tries to use as small a dose as possible. Using doses of 10 - 100 microcuries which delivers about 20 reps to the thyroid gland, numerous investigators have studied the uptake of carrier-free radioactive iodine by the thyroid gland and have drawn some rather interesting conclusions.

It has been found that the thyroids of normal or Euthyroid patients pick up 15-40% of the administered dose; hypothyroid patients, less than 15%; hyperthyroid patients greater than 40% (40-80%). This forms the basis for an important diagnostic test and one that can be used in difficult diagnostic problems - e.g. in self-induced thyrotoxicosis (Alimentary Thyrotoxicos) due to exogenous administration of thyroid extract the clinical picture may be indistinguishable from spontaneous thyrotoxicosis. The latter would show high (40-80%) uptake of Il31 whereas former would reveal almost

complete elimination. This might also find use in infants with hypothyroidism or hyperthyrodism where it would be extremely difficult to determine the basal metabolic rate by the routine method.

At the present time, radioactive iodine has become one of the accepted forms of therapy in a diffuse toxic goiter. Toxic adenomas are to be eliminated from this form of therapy as approximately 5% of these prove to be cancer on histologic examination and thus these should be treated by operation.

For diffuse toxic goiter three forms of therapy are available: (a) surgery; (b) medical management using goiterogenic drugs; (c) radioactive iodine. It is not our purpose here to evaluate all forms of therapy. However, it would be proper to give some of the statistics based on results of treatment with I¹³¹. To date about one thousand cases have been treated. In 90% of the cases hyperthyroidism was controlled in two to four months by one or two treatments (75% were cured with 1 treatment and about 75% of remainder were cured in two treatments). Others still remain under observation. The dose administered varies from 100 - 200 microcuries/gm. of estimated gland weight. The type of response obtained compares very favorably with the type of response following an adequate thyroidectomy - with fall of B.M.R. and serum protein bound iodine to normal in one to four months.

It would not be fair to complete this discussion without mentioning the complications to treatment. About 3% of patients develop transient hypothyroidism which does not require any therapy. About 1% develop permanent hypothyroidism easily contolled with thyroid extract. The problem of long-term effects e.g. production of carcinoma due to the radiation has been proposed as a possible objection to this form of therapy. To date none has been seen but, of course, long-term follow-up is necessary; on the basis of X-ray experience, it is not expected that these will be found. It is to be noted that there is a zero mortality and no effect on the parathyroid glands and vocal cords. These complications compare very favorably with other forms of therapy. However, until long-term follow-up data becomes available, cases for such treatment must be selected carefully. Those most suitable would fall into the following categories:

- (a) Recurrent hyperthyroidism after medical or surgical management.
- (b) Over age of 45.
- (c) Hyperthyroidism with complicating disease.

Carcinoma of the thyroid gland is a rare disease. Primary carcinoma without evidence of metastases should be treated surgically. The following discussion will be confined to carcinoma of the thyroid gland with metastases.

In the groups of cases reported in the literature it has been found that most metastatic foci pick up I^{131} rather poorly - depending upon the type of carcinoma and its differentiation. That is whereas we would expect to get 20 - 40% pick up if it acted like normal thyroid gland, the amount taken up is in the neighborhood of about 1%.

To get around this question of pickup, Seidlin and his co-workers studied a series of metastatic thyroid cancers in which they used thyroidectomy and thyrotropic stimulating hormone in an attempt to induce metastatic foci to pick up I¹³¹. Their results indicate that whereas a tumor might not take up radioactive iodine initially, the stimulation by thyroidectomy and thyrotropic stimulating hormone may cause pickup. Furthermore, they noted a cyclical uptake so that if there is no success, a second trail might show larger pickup.

Using does of 100 to 700 millicuries very large doses of radiation can be delivered to metastatic foci as large as 500,000 reps - amounts which could not be delivered with external radiation without burning the skin.

Using these techniques one can produce a dramatic improvement in the status of an occasional patient with this otherwise uniformly fatal disease. In the presence of carcinoma of the thyroid gland and metastases, there is nothing else to offer. Thus even an occasional remission is worth this effort.

The question of danger to physicians, nurses and other attendants of the patients so treated has been raised. In cases of hyperthyroidism where 3 to 7 millicuries are used, the danger is minimal. There is no escape of beta rays; the intensity of gamma rays escaping from the patient is very low. At 2 meters gamma ray intensity is 0.6 x 10-4 r/hr per millicure. In 24 hours from 3 mc. dose is .004 r at 2 meters so that as far as the treatment of hperthyroidism is concerned, there is no danger to any of the attendants, nurses or doctors. On the other hand, patients treated for metastatic carcinoma usually receive large doses - hence their urine is highly radioactive and they themselves present a slight hazard so that usual radiological safety precautions should be taken. These patients should be kept isolated and their urine handled with 20 to 30 centimeter tongs.

Another isotope which has received considerable attention is P32. This isotope of phosphorus which emits only a beta ray of maximum energy 1.69 Mev. has been used in the form of sodium dihydrogen phosphate since 1936 in the treatment of chronic leukemia and polycythemia vera. The use of P32 in these diseases is based upon the fact that in the bukemia tissue and bone marrow there is some degree of selective localization, therefore selective radiation. However, the degree of selective localization is not so great as would be desirable. Its main advantage over spray x-radiation is that it can be given more easily in centers equipped to do so and does not produce radiation sickness which spray radiation does.

Patients with Polycythemia Vera or Erythremia have been found to receive marked benefit from treatment with P³². The obvious treatment in this disease, since the cause is unknown, is either to remove the excess blood by repeated versection or to control the formation of blood by either x-ray, P³² or chemical agents toxic to the bone marrow such as phenylhydrazine. Since one is attempting to control the formation of red cells, and since the life of the red cells is long - about 120 days - the dosage schedule is to treat the patient with 3-7 millicuries I.V. This should be repeated every three to four weeks for effect as it takes this long before one can notice an obvious trend in red cell formation. Using this or similar schedules, several hundred patients have been treated and the results have been reported in the literature - about 80% are relieved of their symptoms - about 85% obtain a satisfactory hematological remission which in the majority lasts from 1/2 to 5 years and then may require further treatment.

The complications to this form of therapy are overtreatment with the development of leukopenia, thrombocytopenia and anemia. Therefore, patients' blood counts must be followed in first few weeks of treatment rather carefully. A higher incidence of <u>acute</u> leukemias has been reported in patients so treated; however, this is very difficult to evaluate as prior to P32 treatment 10% of patients with polycythemia vera died with blood picture of leukemia (acute and chronic). The cases reported after P32 treatment may thus represent the normal incidence in this disease. The exact significance must await further study.

The demonstration that the uptake of P³² by rapidly growing leukemic cells is considerably higher than the uptake of normal cells led to the investigation of the therapeutic possibilities in leukemia.

The initial dose is 1-3 millicuries (less than in polycythemia vera - as one does not want to affect the red cells) and thereafter 0.5 to 2.0 mc. biweekly for effect. The interval between successive treatments is shorter than in polycythemia vera as the life of the white blood cells is about two to five days. Furthermore, the erythroid elements appear to be more radio-resistant in these conditions than in polycythemia vera.

The results obtained for the treatment of chronic myelogenous and chronic lymphatic leukemias are very similar to the results of x-ray therapy, essentially palliative, not curative but capable of producing remissions. Other blood dyscrasias have been studied but only occasional benefit has been reported.

Since P32 emits only a beta ray with a range of penetration in tissue of several millimeters (half penetration approximately one millimeter) it is being used at present experimentally in treating skin cancers. Theoretically, it would appear quite useful and superior to x-ray or radium since it would avoid irradiation of the deeper uninvolved tissues. There are too few results to draw conclusions at present.

The deposition of P³² in superficial tissues of patients suffering from melanoma and carcinoma has been investigated. Both the rate of uptake and elimination were different than normal skin - suggesting a more active metabolism. After an injection of a small dose of P³², it was found that if the radioactivity over the surface of various types of breast tumors lying very close to the skin were measured, the activity was 25% or more greater on the side of the malignant tumor than in a comparable normal; and slowly growing nucoid carcinometa. In benign conditions this difference was less than 25%. Accordingly, Low-Beer proposed this as a diagnostic test in differtial diagnosis of breast tumors.

During the war the radioactive isotopes of the noble gases were employed to study the problems of decompression sickness. The in vivo technique was used in an attempt to evaluate the factors responsible for the "bends". The results of these extensive and detailed studies indicate that the limiting factor of inert gas exchange is the blood tissue perfusion rates and not the diffusion rates and capillary permeability to the labeled gas.

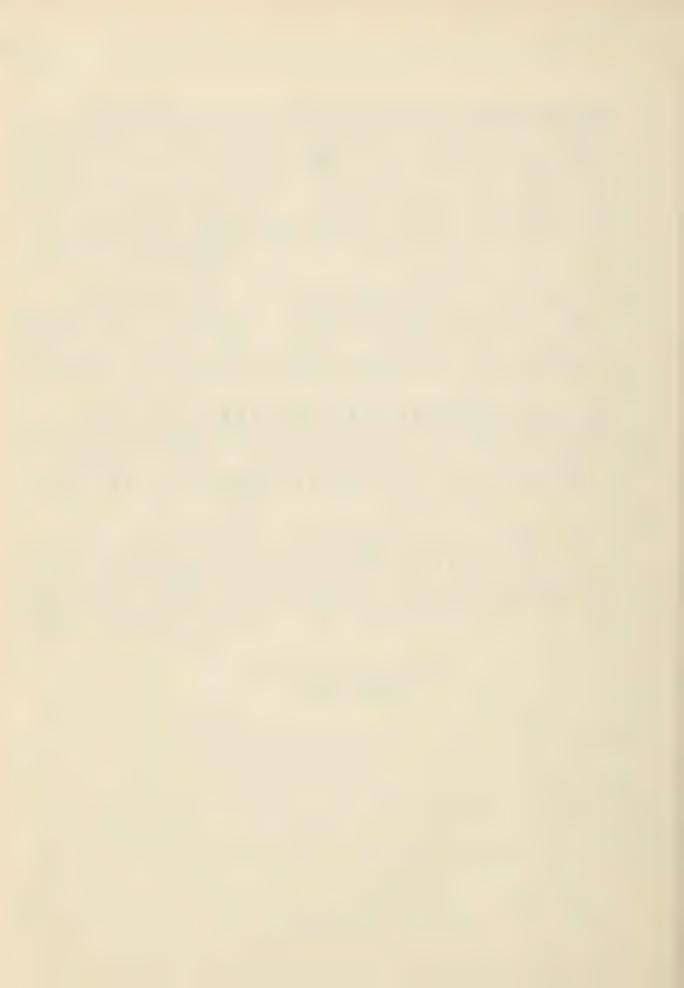
Diodofluorescein has recently been found to concentrate many times in brain tumors compared with normal brain tissue. When this compound is labeled with radioactive iodine, the tumor will then be tagged with radioactivity and if directional counters are used, tumors can then be localized with more certainty. This method originally suggested by Moore and his associates is under investigation at present in many clinics — and looks promising as an advance in diagnostic aid to the neurosurgeon.

From this discussion it is obvious that the field is a very broad one although the practical applications are somewhat limited at present. It is also apparent that the use of these isotopes requires a good deal of thought, careful preparation and evaluation as well as a thorough understanding of instrumentation. With these illustrations, it is hoped that you will each see further clinical applications of these new radioactive isotopes in your particular fields of endeavor.

TRACER TECHNIQUES

by

Captain John R. Hogness
Medical Corps



TRACER TECHNIQUES

Captain John R. Hogness, M. C.

No discussion of the medical aspects of atomic energy can be complete without some mention of the use of radioactive isotopes as tracers, for it is in this field that the greatest advances in medical science resulting from the work on the atomic bomb have so far occurred. It is the purpose of this discussion to present, in very general terms, some of the techniques applicable to the use of isotopic tracers in the field of biology. It is hoped that by pointing out a few specific examples, applications of these techniques in various fields of medical interest may be seen.

First let us define what we mean by a tracer substance. An isotopic tracer is an isotope of an element substituted for a "normal" atom of the same element and introduced into a biological system either as the element itself or as one of the constituents of a given compound. Such an isotope behaves the same as a "normal" atom chemically and in the body. However, because of certain physical characteristics, either radioactive disintigration or a slight difference in mass (in the case of the stable isotopes), we are able to distinguish these atoms in the laboratory, whereas the body cannot. Hence, by knowing that a molecule is "tagged" with an isotope, we can trace the course of that molecule through a biological system.

As an illustration, let us suppose that a wolf pack has been discovered in a given region. By some means we manage to catch one wolf. We paint him with luminous paint and then release him. If on any future night we see this luminous wolf, then knowning that wolves travel in packs, we know that the entire pack is in the vicinity.

Similarly, we may "tag" a compound and administer it to a living organism. Because of its peculiar properties we can then follow its course through various stages of metabolism in the organism.

Radioactive isotopes of a large proportion of the elements essential to life, namely, hydrogen, carbon, sodium, phosphorus, sulfur, chlorine, potassium, calcium, iron, cobolt, copper, zinc and iodine, can now be produced in the atomic pile or the cyclotron, Many of these are available for research and therapeutic purposes. However, for administration to human beings, only isotopes with a suitable half-life or excretion rate or a combination of these two (expressed as the "biological half-life") may be used. Radioactive isotopes which deposit in tissue and remain for long periods of time are undesireable because of the production of long term irradiation effects and the possibility of the development of malignant degeneration.

The Production of Tracer Compounds

As mentioned before, isotopes may be used in tracer work as the element itself, as in the case of Sodium²⁴ in studies of circulation and

sodium space. More commonly, however, such an isotope is incorporated into a give molecule and by its presence, the course of this molecule traced throughout a biological system. For example, urea may be synthesized using radioactive Carbon as the carbon atom in the molecule, and the fate of this compound studied in animals.

Such "tagged" compounds may be prepared for use in two main ways:

1. Chemical Synthesis. Ordinary methods of organic synthesis as carried out by an organic chemist in the laboratory may be adapted to the synthesis of radioactive compounds. Special micro-techniques and radiochemical precautions are essential, however, in the application of organic synthetic procedures to work with radioisotopes. Most compounds now available in this new field have been produced in the laboratory by such means.

2. Biosynthesis.

- a. Animal synthesis.

 Some compounds useful in research are not readily made in the laboratory but are synthesized by animals in the course of their normal metabolic processes. In such cases, it is simpler to administer the isotope to an animal in a simple and readily obtainable form and then isolate the metabolic product from the animal. Such a metabolite will, then, be "labeled" with the isotope administered and may be purified and used in further research.
- As in the case of animals, plants and micro-organisms may also be used to synthesize "tagged" compounds. Again, the isotope is made available to the organism as part of the nutrient medium (including the surrounding air), and the "tagged" compound is later isolated from the organism. The utilization of animals, plants, and micro-organisms in the synthesis of tagged compounds is still in its infancy but this technique will probably be used to a far greater extent in the near future. One of the major difficulties with this method is that it is usually impossible to control the relative position of the isotope in the chemical structure of the compound synthesized in this fashion. The fact that such synthesis must be carried out in closed systems, for the most part, provides a serious drawback in large scale work of this nature.

Let us now assume, however, that by one of these three methods, probably the first, we have obtained a radioactive, "labeled" compound - perhaps a vitamin containing radioactive Carbon 4 and wish to study its metabolic path in an animal. How might we approach the problem?

Gross Metabolism Studies

In studying the fate of a drug in an animal, it is first necessary to determine the amount of the drug or its metabolites excreted in the urine, feces, and exhaled air as well as the amount present in the various body tissues as a function of time; in other words, the "gross metabolism". Suppose then, we administer the Cl4 labeled vitamin to a series of mice, place them in a closed system and collect urine, feces and CO₂. At various time intervals, the animals are sacrificed and the various organs and tissues removed. All these products as well as the tissues are then analyzed for radioactivity. In the case of compounds containing Carbon this may be done in one of several ways. Body fluids such as urine or plasma, or extracts of such products as feces may be plated directly onto planchets and the activity determined with an electronic counting apparatus (see Assay, below). The exhaled CO₂ may be absorbed in NaOH and then precipitated with barium chloride as barium carbonate. This precipitate may then be analyzed for radioactivity.

Perhaps the most commonly used technique for analyzing for C¹⁴ is that of combustion. This method involves the burning of all organic material to CO₂ and collection and precipitation as mentioned above under "exhaled CO₂". This technique is applicable to all organic materials, but is especially useful in analysis of C¹⁴ activity in tissues.

Thus we see how a gross metabolism study in the case of a Carbon containing compound might be carried out. By determining the amount of radioactivity present in any of the excretory products or tissues we know the fraction of the originally administered compound or its metabolites present. Compounds containing other isotopes would each require special techniques or modifications of the above methods, depending upon the element and the type of radiation involved.

Assay of Radioactive Materials

In order that those studies mentioned above may be carried out on a quantitative basis, it is necessary that the originally administered compound as well as the final products and tissues be assayed accurately for the amount of radioactivity each contains. The determination of radioactivity in a specific substance depends upon the isotope involved, or more specifically, the properties of the radioactive particles emitted by that isotope.

A discussion of various types of instruments has already been presented. However, in general, those isotopes emitting beta and gamma rays may be assayed with a system employing a Geiger-Muller tube as its essential unit, the thickness of the wall of the tube in each case being dependent upon the energy and penetrating ability of the beta or gamma ray involved. Carbon for example since it emits a very weak beta particle, requires a Geiger-Muller tube with a thin mica window for assay work. Alpha

emitters, because of the extremely low penetrating power and high ionizing power of the alpha particles, require an instrument of the "proportional counter" type. Alpha emission is encountered for the most part among the heavier elements, especially those involved in the processes of fission.

In the case of the stable isotopes, where there is no radioactivity involved, analysis must be made on the basis of slight differences in mass between isotopes. Assay in this instance becomes far more difficult and time consuming. Various methods of analysis have been developed, the commonest technique being that involving the use of the mass spectrometer.

Radioautographs

Once the gross distribution of radioactivity in the body has been determined, it is of interest to attempt to localize the radioactive material within the specific tissue. For this purpose the technique of radioautography (or autoradiography) is extremely useful.

Radioautography implies that the tissue (or other substance) containing radioactive material takes a picture of itself. This is, in fact, precisely what occurs. The various emanations from radioactive materials will, like x-rays, darken photographic plates. Thus, when a section of tissue containing a radioactive substance is placed in contact with a photographic film, allowed to remain in contact for a suitable exposure time and the film then developed, darkening will be apparent on the film in the areas corresponding to those where radioactivity was present in the tissue.

Again, take the example of the mouse injected with a radioactive Carbon "tagged" vitamin. Assume this compound is present in the kidney (among other organs) and we wish to know just where in the kidney the vitamin is located. We can make a tissue section and place it next to a photographic film. After leaving the film and tissue in contact for a period of several weeks, we then develop the film. It is possible to compare the dark, exposed, areas on the film with the tissue section and, correllating these, pick out the part of the tissue from which radiation was emanating and hence the area in which the vitamin or its metabolite is located.

There are, in general, three modifications of radioautographic technique in use at present, each having its own application.

a. The tissue section may be mounted on a glass slide in the ordinary manner, and the photographic film brought in close contact with the slide and fixed in position during the exposure period. This technique has the disadvantages that the tissue is not in as close approximation to the film as might be desired, and also that once developed, the film and the tissue section must be viewed separately rather than simultaneously, under the same microscope. It has the advantage that after exposure the tissue section may be stained without fear of affecting the emulsion.

- b. The tissue section may be mounted directly on the film itself where it will adhere very firmly. Following exposure and development of the film (with the tissue still adherent), it will be possible to focus through the tissue to the film and thus view both simultaneously.
- c. A third method of making radioautographs involves the spreading of photographic emulsions directly over the tissue mounted on a slide. This provides very close contact between tissue and emulsion but presents difficulties in staining the section of tissue afterwards.

In some instances in the making of radioautographs, using special emulsions, it is possible to distinguish not only darkened areas but definite tracks on the emulsion made by the particules given off by radioactive substances. By tracing several of these tracks back to a common point source, it may be possible to localize one individual radioactive atom in a specific part of one cell. This technique is particularly applicable in the case of alpha emitters having a long decay chain. Recently emulsions have been developed on which beta particles will produce tracks.

Radioautography has numerous applications in radiobiology, a few examples being in tracing iodine uptake by the thyroid gland, in the localization of strontium as well as plutonium and other heavy metals in bone, and in studying sodium exchange in the eye.

Filter Paper Chromatography

Another very useful technique in tracer work is that of filter paper chromatography. Chromatography as such was first used about one hundred years ago as a method of separating mixtures of various materials. More recently, this technique has been adapted for use in the separation of small amounts of radioactive compounds, by using long strips of filter paper in place of the customary absorption columns.

Briefly, the technique is as follows. Long strips of filter paper are suspended inside airtight columns, the upper end of the strip being dipped into a solvent system such as, for example, a saturated solution of butanol in water. The air in the column is also saturated with the vapor phase of this system. A drop of solution containing the radioactive materials to be separated is then placed on the filter paper strip just down the strip from the point where it is immersed in the solvent system. Then, as the solvent runs down the filter paper by wick action, the various radioactive components spread out on the strip according to their differential solubilities in the solvent, the most soluble migrating the fastest and the least soluble the slowest. These compounds are therefore effectively separated according to their solubilities. The strip is then dried and placed in contact with an x-ray film for a suitable period and a radioautograph of the strip is made. By examining the autograph, it is

possible to determine the number of radioactive compounds present and their location along the strip. From this point on, it is necessary to identify each radioactive band on the strip. This can be done chemically, by utilizing the physical properties of the individual components, or occasionally by bacterial assay.

Filter paper chromatography has been used in such problems as the separation of amino acids in tissue hydrolysates or plasma and the separation of metabolities of drugs in the urine and other body fluids and tissues.

Examples of Applications of Tracer Technique

It will perhaps be interesting and instructive to cite a few examples of biological tracer studies already carried out. From these examples it is hoped that possible applications in other fields may be suggested.

In the clinical field the applications of radioactive tracers are very extensive and the possibilities are greater still. Some examples of these applications such as the use of Sodium²⁴ in studies of circulation and body sodium space and the use of Iodine¹³¹ in studies of thyroid metabolism have already been mentioned. Other clinical applications include the use of radioactive sodium in studies of sodium exchange across body membranes, the use of radioactive iron in studies of red cell life and circulation, the use of Iodine¹³¹ in studies of organic iodine turnover in the body, and the use of deuterium and possibly tritium (H³) in body water studies.

The applications of tracer techniques to animal work are even more extensive than in clinical investigation because the number of isotopes that can be used safely in humans is quite limited. Much of the work done with animals concerns studies of the fate of drugs and other compounds in the body as well as determinations of the rate and mechanisms of synthesis of various body compounds. One example of the former type of study is the tracing of "tagged" vitamins mentioned previously. Examples of the latter type include the administration of "tagged" acetate to animals and the study of its utilization in the formation of body cholesterol, as well as the use of Phosphorus 32 in studies of the fate and synthesis of nucleic acids and nucleoproteins.

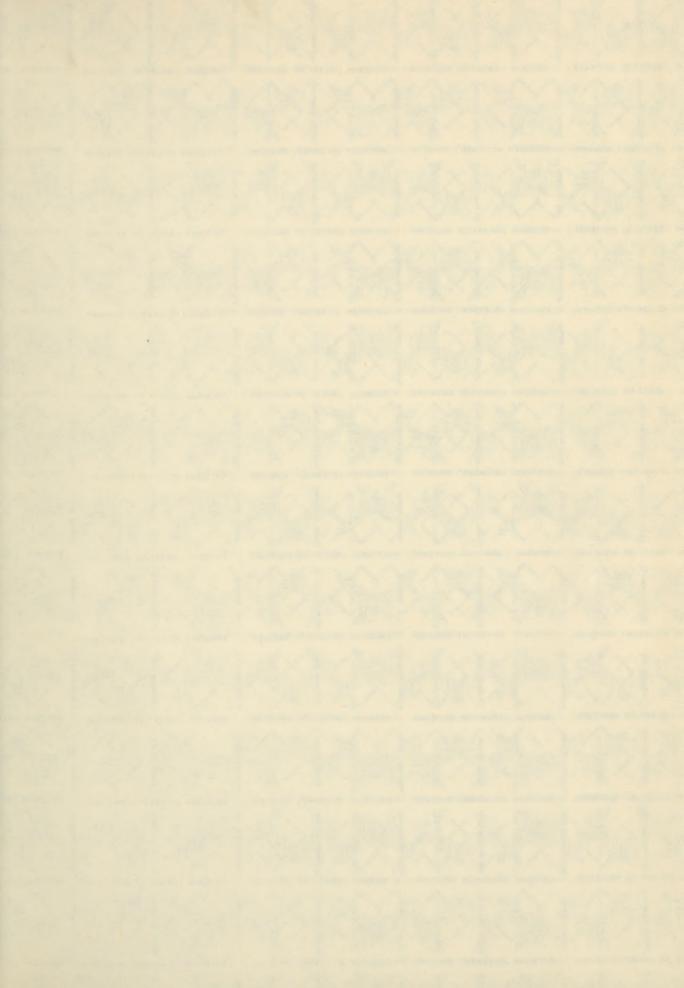
Tracer materials offer an important new tool to the bio-medical investigator. Many significant advances have been made in the past three or four years through the use of isotope tracer techniques but the surface has barely been scratched.



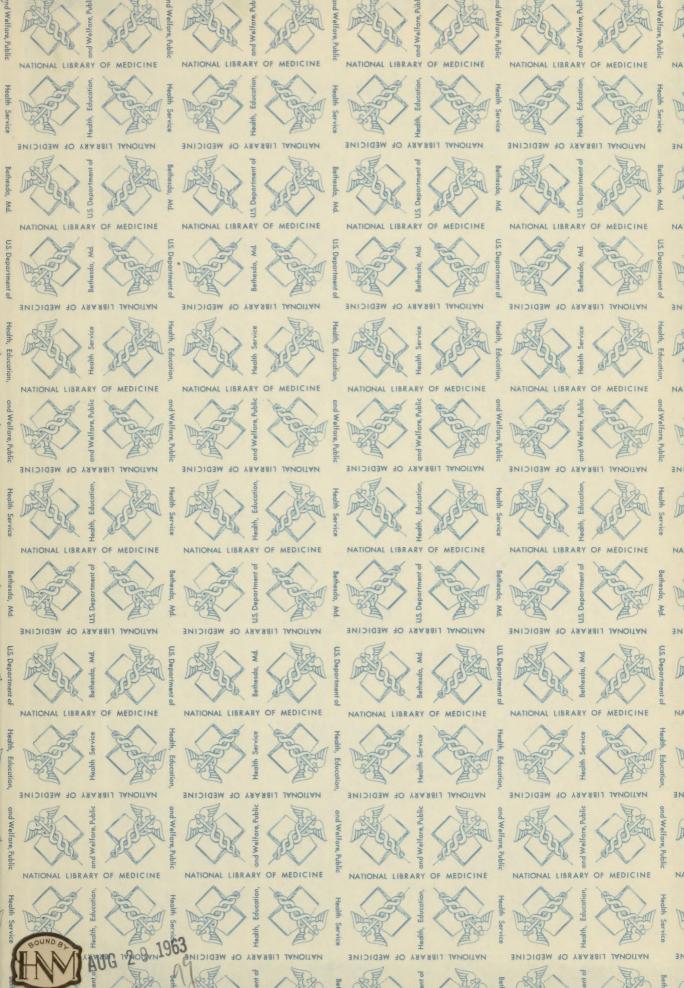












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